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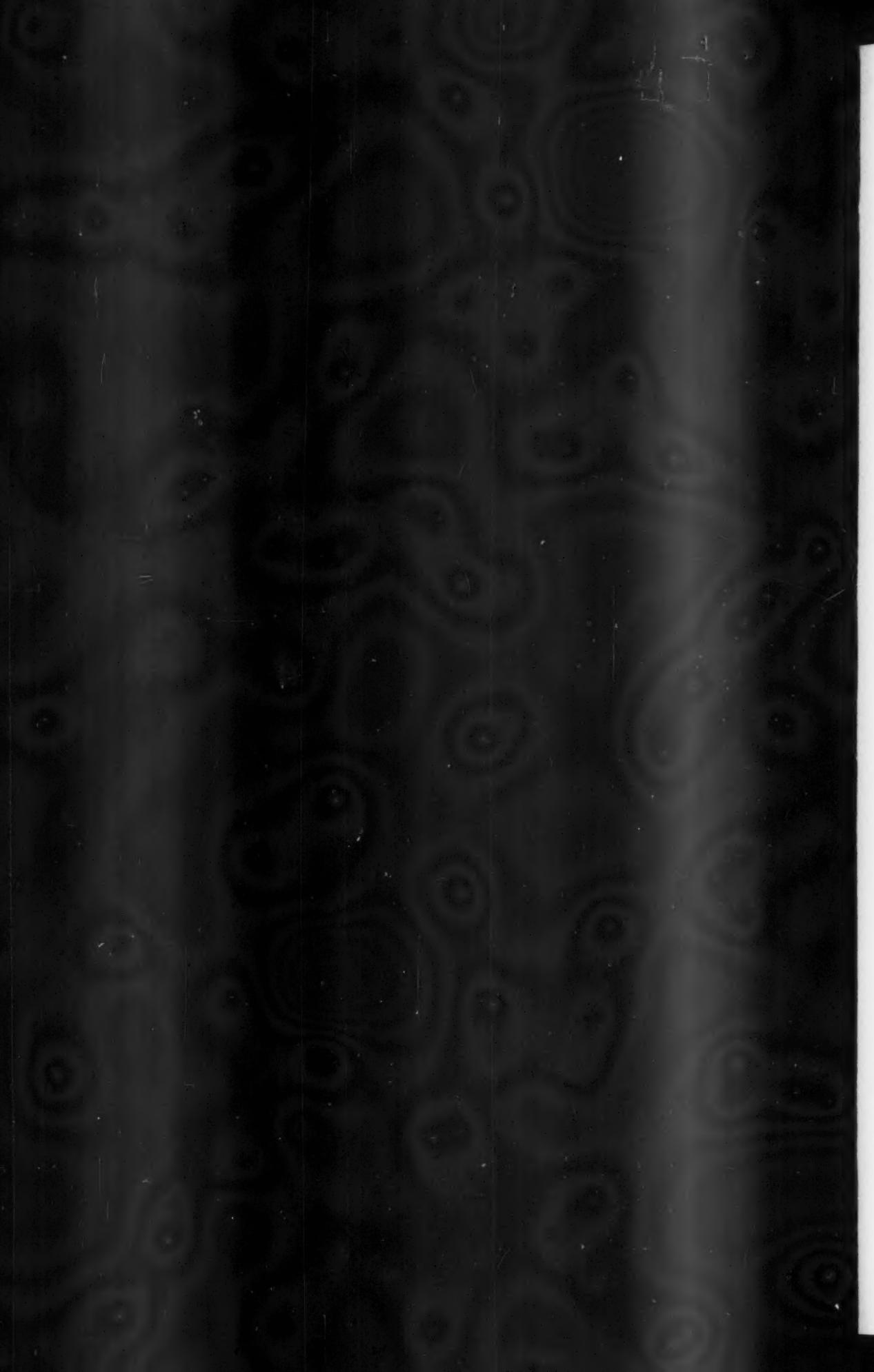
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Original Communications

OVARIAN FIBROMAS: A CLINICAL AND PATHOLOGIC STUDY OF TWO HUNDRED AND EIGHTY-THREE CASES

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EXACTLY two hundred years have elapsed since Astruc¹ in 1743 gave to the medical literature the first description of an ovarian fibroma. He emphasized the rarity of this type of tumor. For the next hundred and forty years isolated articles on the subject dealt mainly with certain gross pathologic changes which were seemingly peculiar to this neoplasm, to whose clinical manifestations very little attention was directed. In 1882, Coe² in an excellent review studied the histogenesis of ovarian fibromas, deciding that they represented an overgrowth of the ovarian stroma. He observed the frequent occurrence of edema in the tumor substance and correlated its presence with the formation of "geodes" or degenerative cysts. Twenty years later, in 1902, Peterson¹³ in a succinct review first correlated clinical and pathologic data from reports of a total of eighty-two cases found in the literature and from a careful study of two cases of his own. He remarked on the slow clinical evolution of these tumors, and, pathologically, the relative absence of adhesions with a notable incidence of ascites. Peterson's investigations stimulated interest on the part of others and from 1902 to 1920 fibromas "came into their own," so to speak.⁵ Accordingly it became apparent that (1) ovarian fibromas were not in fact pathologic curiosities; (2) they were by no means clinically silent.

Another spark of enthusiasm was touched off by Meigs and Cass.¹¹ These investigators pointed out that ovarian fibromas, although essentially benign in their evolution, sometimes produce clinical hydrothorax in addition to ascites. "Meigs' syndrome"^{2, 9} now embodies the

NOTE: The Editors accept no responsibility for the views and statements of authors as published in their "Original Communications."

clinical triad of ovarian fibroma, ascites and hydrothorax—a combination which in the past had been interpreted all too frequently in terms of "inoperable malignancy."

Finally, no review, however brief, would be complete without reference to the theca-cell tumor described in 1932 by Löffler and Priesel.¹⁰ These investigators discovered that certain "fatty fibromas" were associated notoriously with periodic postmenopausal bleeding. The separation of the members of this "functioning" or theca-cell class from the general group of fibromas wrote a new chapter in gynecologic pathology. From our standpoint, it was felt that a clinical and pathologic analysis of a relatively large group of patients who had ovarian fibromas might throw some light on the incidence, histogenesis, complications and so forth, of this much neglected type of tumor.

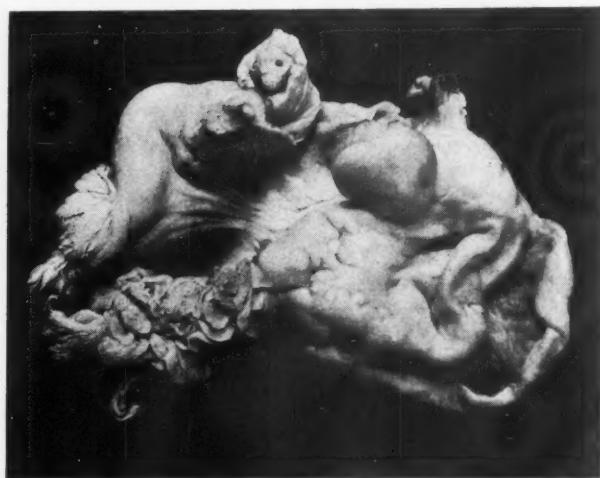


Fig. 1.—A small fibroma is seen springing from the ovarian cortex.

Materials and Methods

Records from the Division of Surgical Pathology and the section on pathologic anatomy of the Mayo Clinic were examined carefully for tumors bearing the designation fibroma, fibromyoma, fibroblastoma, xanthofibroma and so forth, affecting the ovary. Approximately 350 tumors included under these headings had been found at surgical exploration or at necropsy on patients seen at the clinic from 1907 to 1942, inclusive. Pathologic material was next secured and the tumors were studied in gross detail for data pertinent as to side, size, color, consistency, degree of encapsulation, edema, formation of cysts, and so forth. Associated pathologic lesions of the uterus and Fallopian tubes were recorded when these tissues were present. These data were all recorded carefully on specially prepared cards. Multiple blocks were then cut from the tumors and attempts were made to select regions which included also (in the same block) material from any identifiable ovarian substance. These blocks were placed in a fresh 10 per cent solution of commercial formalin, cut at a thickness of 10 microns on a freezing microtome, and stained routinely with hematoxylin and eosin. When

indicated, special stains such as the Galantha strain for mucin, sudan III stain, and the van Gieson stain for hyaline substance were also employed. Several thousand sections were thus made available for study. Preliminary microscopic "scouting" eliminated the occasional examples of granulosa tumor, theca-cell tumor, Krukenberg tumor and Brenner tumor from the series. A fair number of adenofibromas was found and similarly deleted. Three hundred and twelve "residual" ovarian fibromas (Fig. 1), occurring in a group of 283 patients, constitute the basis of this report.*

Clinical Features

Incidence.—The incidence of fibromas was ascertained to be slightly more than 5 per cent of all surgically removed ovarian tumors. Because the comparison did not include cases of inoperable pelvic malignant lesions of undoubted ovarian origin this figure of 5 per cent is somewhat higher than that which actually exists. Rhodenburg¹⁴ found the incidence of ovarian fibromas to be 5 per cent; Hellman⁷ expressed the opinion that an incidence of 2 per cent is more nearly correct.

Age of Patients.—The average age of patients who had ovarian fibromas was forty-eight years; the age of the youngest was sixteen and of the oldest was seventy-nine years, respectively. No patients were in the first decade, the second accounted for two, the third decade for nineteen, the fourth for fifty-one and the fifth for seventy-five. The sixth decade led the list with eighty-eight patients while forty-two patients were in the seventh and six in the eighth decades, respectively. Thus 31 per cent of the patients were from fifty to fifty-nine years of age, inclusive—an incidence for the sixth decade which agreed well with the figure of 28 per cent cited by Peterson¹³ in his review. Our failure to find ovarian fibromas in the prepubertal age group of patients paralleled the observations of others and perhaps lent some support to the hypothesis of origin conceived by Brothers,³ namely, that the hemorrhage attendant upon ovulation might be a significant "inciting agent" in the development of these tumors.

Marriage and Pregnancy.—Forty-three of the patients were single, 233 were married and in seven cases the civil state was not mentioned on the record. Of the married patients 185 had given birth to one or more children for a total of 503. Forty-three of the patients had been described as "childless" and in five cases information on this family item was not available. Accordingly, in the present series, as with others reported in the literature, evidence was lacking that the development of fibroma influenced the parity of the patient or was influenced by it. On the other hand, it should be recalled that the majority of fibromas became clinically manifest after the climacterium.

Complaints.—The commonest presenting complaint was the presence of a tumor. Eighty-eight patients had noted this symptom for an average period of thirty-three months with extremes of one week and thirty years marking the "time limits." The tumors were described generally as being of slow growth but a few of the patients had observed episodic increases of the size of their abdominal masses. Frequently these episodes were associated with the development of pelvic pain. However, forty-five patients in this group described the evolution of their tumors as being painless and in the remainder pain was frequently not very severe. Twelve patients had noted that the mass shifted with certain

*Fifty-five of these tumors were reported previously by Hoon.⁸

shifts of body position. (However, this phenomenon has been observed also among patients who have ovarian cysts and uterine fibromyomas).

Pain was the principal complaint listed in the records of seventy-nine patients. In general, it did not have any diagnostic features. In thirty-six cases, it was present as the sole complaint, and in forty-three, it was noted in association with a tumor mass. In twenty-one cases the pain was more or less dragging, was located in the lower portion of the abdomen or in the flanks, and usually was without extension. In fifty-eight instances it was sharp, coming on in attacks. In no less than forty-nine of this latter group of cases, there was ascites or adhesions or both plus a noteworthy incidence of an edematous, twisted tumor pedicle. The latter was adjudged accordingly as an important etiologic factor in the production of pain.

Symptoms referable to interference with urinary function (frequency, nocturia and dysuria) occurred either alone or in combination with other symptoms in forty cases in this series. These urinary difficulties appeared to be related to ovarian fibromas of an average large size but did not differ otherwise from the similar disturbances noted among patients who had ovarian cysts. Their basis appeared to be mechanical compression of the urinary bladder. Backache, "pelvic pressure," "piles" and "varicose veins" were included in a long list of incidental symptoms with a similar etiologic basis. In 138 of the records, the listed symptoms were ascertained to have had no relation to the presence of the ovarian fibroma (usually small). They were produced by the "associated pathologic lesions" described elsewhere in this paper. These symptoms included "irregularity of menstrual flow," which in our analysis rarely could be attributed to the presence of an ovarian fibroid. The discovery of seven theca-cell tumors in our original group easily explained the phenomenon of periodic post-menopausal bleeding associated with certain atypical tumors.

Physical Findings.—Although the clinical diagnosis of "fibroid" was made in fifty instances, in only a few was the designation "ovarian" appended. In the case of larger neoplasms the notations "ovarian tumor with ascites," "ovarian cyst," "movable pelvic-abdominal tumor" and so forth appeared. In twenty-five instances a twist of the tumor pedicle was believed to exist. In twenty instances the presence of abdominal ascites was demonstrated and fairly frequently resulted in the notation "malignant." In two of these cases concomitant hydrothorax was apparent. With many of the symptomless fibromas the conditions indexed referred to the "associated pathologic lesions."

Laboratory data did not contribute any pertinent diagnostic information. Roentgenographic studies, including the occasionally indicated simple roentgenogram, although frequently demonstrating the presence of a soft-tissue shadow in the pelvis, rarely led to the identification of the type of tumor.

In summarizing the foregoing data we might say briefly: Small ovarian fibromas (those less than 4 cm. in diameter) rarely produce clinical symptoms. Large ovarian fibromas duplicate the clinical picture of any slowly growing pelvic tumor plus an unusually high incidence of ascites. A moderate degree of mobility and a firm consistency of fibromas predispose to twisting of the pedicle of the tumor with consequent pain. In the absence of infallible clinical signs, the diagnostic issue must be settled by surgical exploration of the pelvis. To decide otherwise denies the benefit of cure to many patients in whom

the presence of ascites suggests the existence of an inoperable malignant process.

The treatment of fibromas of the ovary is always surgical and no matter how small a solid tumor of the ovary is when first recognized, removal should be advised, as the possibility of a malignant lesion must always be considered and can be ruled out only by examination of the growth. The other ovary should always be examined carefully, as the possibility of other smaller, similar tumors must always be considered.

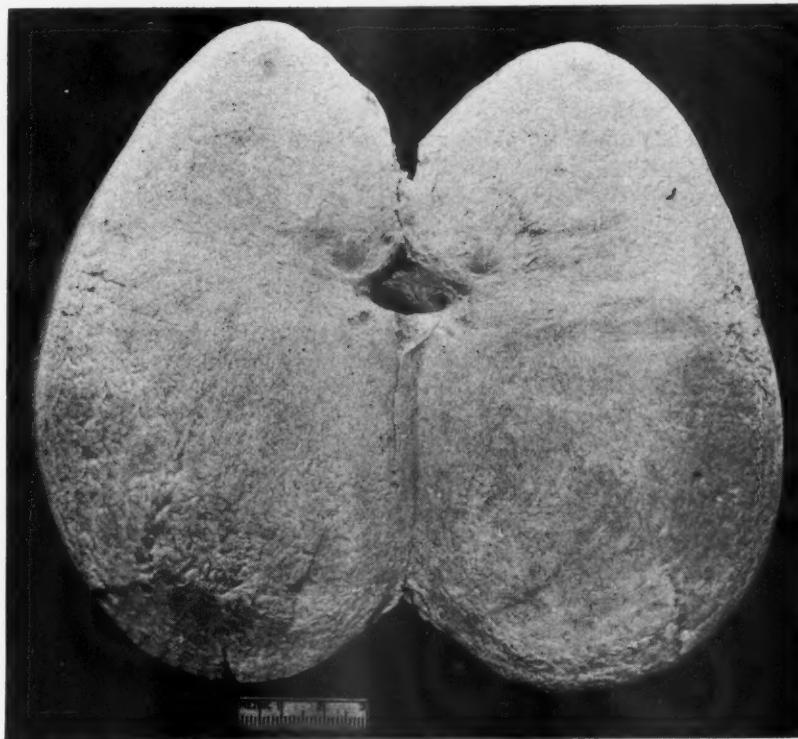


Fig. 2.—Large ovarian fibroma associated with ascites. The white color, fine texture and firm consistency are characteristic.

Pathologic Data

Side of Involvement.—No predilection was noted in this regard, the right and the left ovary showing the same incidence of involvement by fibroma.

Size of Tumor.—The average diameter of 312 tumors surgically removed from the 283 patients in this series was 6 cm., with 141 of the tumors exceeding this dimension. Only fourteen of the tumors could be described as being very large (more than 20 cm.). It was interesting to note that the aforementioned average size, with few exceptions, represented a clinical threshold for the production of symptoms. (Most of the larger tumors probably had "outgrown" their early site within the true pelvis.)

Multiplicity.—In twenty-eight cases (approximately 10 per cent) multiple ovarian fibromas were encountered. Within this group bilateral single tumors occurred in twenty-three instances, bilateral

multiple tumors in two and unilateral multiple fibromas were present in the three remaining cases. These figures are in keeping with those recorded in the literature but, inasmuch as both ovaries were not always available for study, the figures probably represent too low an incidence of bilateral tumor.

Color of Tumor.—Nearly all of the fibromas possessed a whitish or grayish-white color, particularly noticeable on cut section (Fig. 2). In a few instances in which a recent twist of the tumor pedicle had taken place, infarction imparted a reddish hue. A yellow color indicated the existence of fatty metamorphosis, or, as in seven instances noted previously, the necessity for revising the diagnosis to that of theca-cell tumor. The color of ovarian fibromas has long been observed to be so characteristic as to make possible an accurate diagnosis on gross inspection in most instances. Our observations substantiated this view.

Consistency.—Two hundred and sixty of the tumors (83 per cent) were solid throughout and unusually "heavy." In several of our more recent cases rough estimation of the specific gravity corroborated our impression that, per unit of volume, ovarian fibromas rank among the most dense of the tumors of soft tissue. Fifty-two of the tumors were associated with cysts of variable size and position. Surface cysts were usually small and possessed of a smooth lining. Central cysts were more obviously of a degenerative type with ragged, irregular walls. Often-times concomitant edema of the tumor and its pedicle was noted. (These central cysts are the "geodes" of earlier investigators and their significance will be discussed in a subsequent section.) The contents of the cysts usually were clear and watery, occasionally bloodstained, and, in a few instances, "tarry." Ovarian tissue was often grossly identifiable in the neighboring surface cysts.

Ten of the tumors were almost completely calcified and in an additional fifteen, "gritty" foci were encountered in sectioning blocks for microscopic investigation.

Ascites.—Abdominal ascites in amounts calling for a surgical note as to its presence was a complication of fifty-one ovarian fibromas and constituted one of the most interesting features in this study. Never occurring in association with tumors less than 6 cm. in diameter, it "complicated" no less than 36 per cent of fibromas larger than this established average size. The ascitic fluid varied from $\frac{1}{2}$ pint (237 c.c.) to more than 3 gallons (11 liters), the quantity being in general proportionate to the size of the causative tumor. In many instances there was a history of repeated reaccumulations of the fluid following previous paracenteses. In six cases the fluid was blood tinged and in these cases there was evidence of a recent twisting of the pedicle of the tumor. In the remaining cases the fluid was clear and chemically appeared to represent a transudate rather than an exudate. In two cases there was concomitant hydrothorax. In a combined clinical and pathologic search for the etiologic "common denominator" producing ascites the following facts appeared to be pertinent: Edema of the tumor or its pedicle or both was present in thirty-one of the fifty-one cases in which there was ascites. (This incidence of edema was twice that observed in the group without ascites.) Central cystic degeneration with or without edema was noted frequently in tumors of the "ascitic group" (Fig. 3) but was rare in the group of cases in which free peritoneal fluid was not observed at the time of operation. In 30 per cent of the cases in which there was ascites, adhesions, probably re-

sulting from ancient twists of the pedicle of the tumor, also were present. Pain was an important clinical feature in this latter group.

Microscopic Features.—The microscopic characteristics of ovarian fibroma have been described well by Peterson,¹³ Meigs and Cass¹¹ and

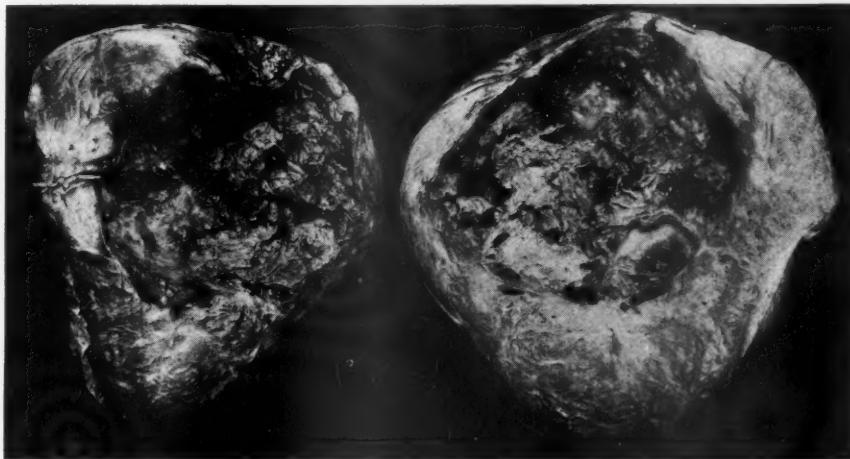


Fig. 3.—Large ovarian tumor associated with ascites. Note the extensive degeneration with formation of cysts.

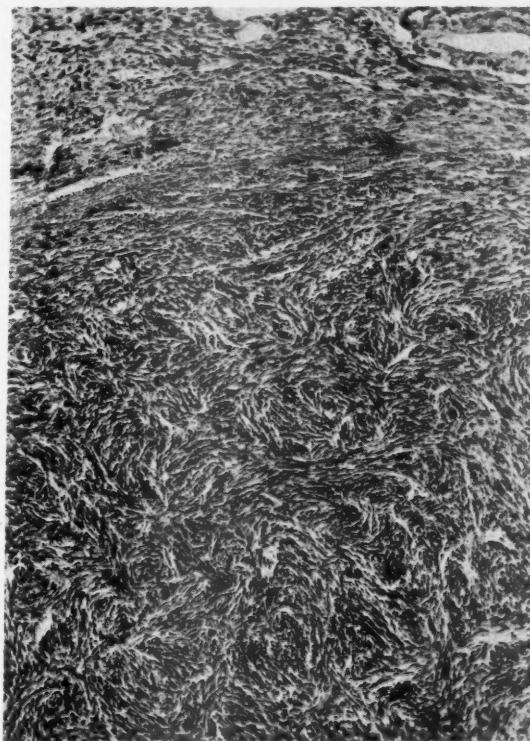


Fig. 4.—The section made from a small cellular fibroma at its junction with the enveloping cortex shows closely packed spindle cells in "featherstitch" arrangement. The line of demarcation between normal and tumorous tissue is not distinct (hematoxylin and eosin $\times 100$).

others. In keeping with their observations, we found that all of the tumors could be classified into cellular and fibrous types occurring in pure or mixed forms. In all, the basic cell appeared to be the peculiar mesodermal type so characteristic of the ovarian stroma. Moreover, the tumors in general preserved the closely knit "featherstitch" arrangement (Fig. 4) so typical of the normal ovary. In general small tumors were cellular, resembling in this respect ovarian cortical stroma.

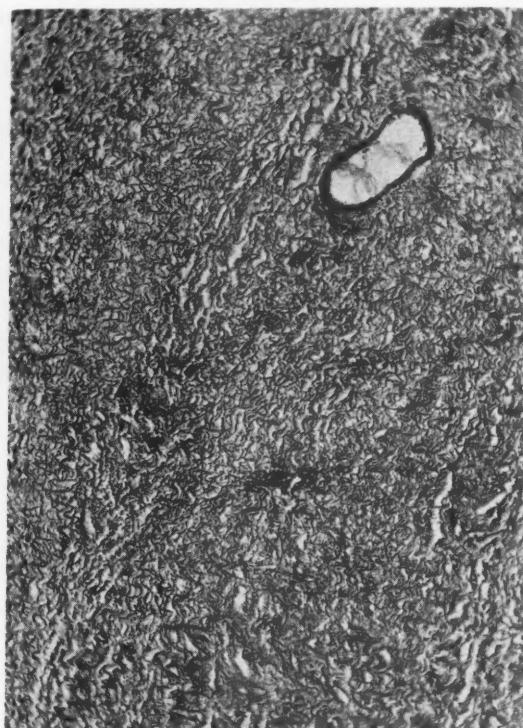


Fig. 5.—Fibrous stroma—poor in cellular elements, rich in collagenous fibers (hematoxylin and eosin $\times 100$).

Large examples on the other hand were frequently fibrous (Fig. 5) and even hyaline, suggesting that deposition of collagenous and hyaline substance represented degenerative or "senescent" changes in the maturation process of a basically cellular type. Individual tumor cells were small, thin, spindle units with pointed cytoplasmic processes and narrow, oval, hyperchromatic nuclei running parallel to the long axis. Collagenous and hyaline material surrounded and compressed the cells in many fields. Moreover the hyaline "bands" which have been described as being typical of theca-cell tumor were encountered fairly frequently. When, as was sometimes the case, fatty metamorphosis existed along with hyaline change, some difficulty was encountered in making a microscopic diagnosis of fibroma versus theca-cell tumor. In many instances the plump appearance of the true theca cells was the deciding factor, but in others the clinical history combined with chemical analysis for type of lipid substances was necessary in order to decide the issue.

Ovarian tissue was identified microscopically in about one-half of the cases studied. The demonstration within this tissue of follicles, corpora

lutea and corpora albicantia served as a reminder that ovarian fibromas are extremely rare (if indeed ever found) before the onset of puberty. In the case of small fibromas a layer of "germinal epithelium" invested both ovary and tumor, but with larger neoplasms the capsular investment was fibrous. In no instance was epithelium of a secretory type found on the surface of a fibroma where it might conceivably give rise to ascites. Cystic fibromas, microscopically, were of two types: (1) small fibromas containing multiple small, smooth-walled, superficial cysts, often bilateral; (2) large fibromas with single or multiple cysts, often of fair size, with rough, ragged walls. In the former condition there was often a lining of flattened granulosa cells. These tumors

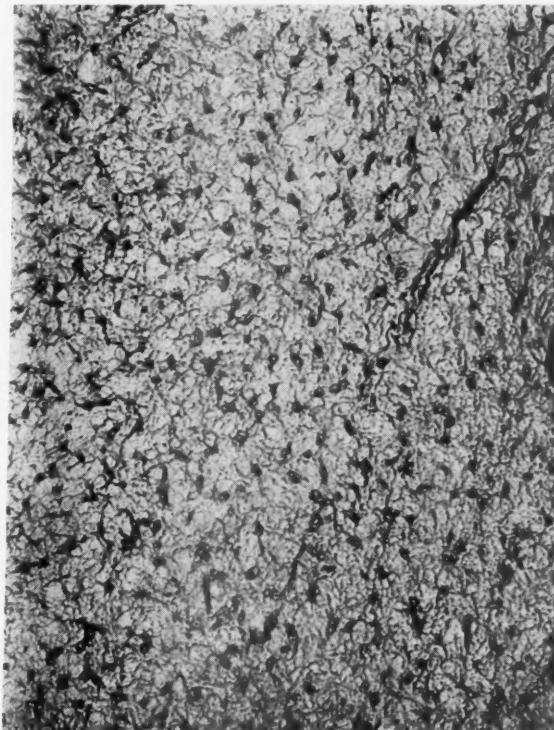


Fig. 6.—The photomicrograph, made from the tumor illustrated in Fig. 2, shows marked separation of the tumor cells by edema fluid. This picture we have found consistently in fibromas producing ascites (hematoxylin and eosin $\times 170$).

might be classified as the end result of fibrous overgrowth affecting the ovary rather than true localized formation of fibroma. In the second group the cysts appeared to arise through a fusion of zones of edema within the tumor substance—the "geodes" of Coe⁶ and other writers on the subject. In the case of large central cysts, even though the walls were sometimes fibrous, interstitial edema was always present in noneystic portions of the tumor.

Including the cases of edema with formation of cysts, the separation of tumor cells by an excess of tissue fluid (Fig. 6) was observed in seventy of the 312 tumors examined. That it was often patchy in distribution, even microscopically, indicated that our observed incidence was probably too low. Significant was the fact that of fifty-one tumors accompanied by production of ascites, forty-nine (96 per cent) showed

edema, usually in marked degree. This appeared in contrast to a 10 per cent incidence of edema in tumors without ascites. Moreover, in this latter group of twenty-seven tumors, although fluid was not present in the "free" state, it was enveloped in thirteen instances within the ragged walls of the degenerative cysts referred to in the foregoing paragraph.

Surface adhesions, present on forty-three tumors, were studied but no positive conclusions were drawn except that the adhesions had resulted from chronic infarction and consequent peritoneal irritation. In several instances such infarction had resulted in the tumors becoming parasitic. In twenty-nine of these forty-three cases there had been a clinical history of attacks of pelvic pain.

Associated pelvic pathologic lesions included a large number of conditions, with uterine fibromyomas leading the list. The ovary in which the fibroma was situated was simultaneously at times the seat of simple cyst, dermoid cyst, tarry cyst, cystadenoma or cystadenocarcinoma, against the development of which fibroma did not confer any apparent immunity. Sarcomatous change was observed in three examples. All three of these cases have been reported previously from the clinic.⁴

Origin of Ovarian Fibroma.—Histogenetic studies carried out principally on tumors of small size indicated that ovarian fibromas arose from the spindle cells of the ovarian cortex. Indeed in many instances it was almost impossible to say definitely just where normal cortex ended and tumor began.* Moreover, as previously indicated, the tumors preserved in fair degree the "featherstitch" pattern of the normal ovarian architecture. Following the hypothesis of Brothers⁵ that ovarian fibromas result from the desmoplastic reaction attendant upon ovarian hemorrhage, a search was conducted for the telltale evidence of hemosiderin pigment. Results were disappointing with positive findings in twenty-three instances only. (However, evidence of old hemorrhage often is not seen in corpora albicantia even though one may be sure that hemorrhage was present in the corpora lutea of origin.) The hemorrhage associated with endometriosis was similarly disappointing in its practical nonappearance but the finding in twenty-five ovarian fibromas of endometrial-like glands indicated a possible stimulation for the formation of fibromas. Twenty-three other tumors, originally listed as fibromas, contained so many glands that they were deleted from the present series, under the caption "adenofibromas." Briefly, then, although our studies did not bear out universally the importance of hemorrhage in the histogenesis of ovarian fibromas, the clinical observation that fibromas did not occur before the age of "ovarian hemorrhage" plus the occasional finding of hemosiderin and endometrial glands in fibromas might be correlating facts of importance favoring such a view.

Summary and Conclusions

Ovarian fibroma is the second commonest of the solid ovarian neoplasms. Three hundred and twelve of these tumors accounted for 5 per cent of all ovarian tumors surgically removed at the Mayo Clinic. Ovarian fibroma was never encountered before the age of puberty and this observation has been taken to indicate an origin possibly based on a

*The so-called fibroma of the corpus albicans appeared in our experience to be a structure totally dissimilar to, and never productive of, true ovarian fibroma.

desmoplastic reaction to the hemorrhage of ovulation or ovarian endometriosis. Fibroma did not produce any specific diagnostic symptoms and rarely was it possible for the clinician to go further than to say "ovarian tumor," "solid ovarian tumor," and so forth. Abdominal ascites (fifty-one cases) and hydrothorax (two cases—syndrome of Meigs) suggested the existence of a malignant process but the patients never presented the picture of cachexia. The complications of these tumors were chiefly those associated with twisting of the pedicle of the tumor—a phenomenon which rarely occurred until the tumor outgrew the confines of the true pelvis.

Pathologically, most of the tumors were solid throughout, white and usually invested by a smooth capsule free from adhesions. Many of the tumors were edematous and a number of these had undergone degenerative changes with central cysts or "geodes." The common denominator relating to both ascites and formation of cysts was a weeping edema effected through partial obstruction of the venous return. Hydrothorax was very rare and appeared to be incidental. (It occasionally occurred from equally obscure causes among patients suffering from ascites of origin other than fibroma.)* In 90 per cent of cases the tumor was unilateral. Bilateral fibroma-like tumors sometimes proved to be metastatic tumors of the Krukenberg type with the primary neoplasm most frequently in the stomach. A yellowish color suggested theca-cell tumor, especially in cases in which the uterus was large and postmenopausal bleeding was noted clinically. In others the yellow color resulted from fatty metamorphosis. A grayish-brown color and firm consistency were noted in several tumors that later proved to be of the Brenner type. A brownish color and soft consistency indicated malignant change, which occurred in 1 per cent of the tumors studied.

Microscopically, both cellular and fibrous types appeared to arise from the spindle cells of the ovarian cortex with hemorrhage as a possible inciting element. Degenerative changes, such as fatty, fibrous, hyaline and calcareous, took positions of importance secondary to the phenomenon of intercellular edema, which correlated more universally than did gross edema and formation of cysts with the clinical production of ascites. Pelvic lesions other than ovarian frequently accompanied fibroma, which at the same time did not protect residual ovarian tissue from the development of dermoids and other tumors.

Addendum

Since we looked up the statistics for this paper, a patient suffering from Meigs' syndrome has been operated upon at the clinic. The report of the case is as follows:

*Meigs and co-workers¹² recently discussed the various hypotheses of origin of ascites from ovarian fibroma. Moreover, in one of their recent cases they demonstrated the apparent ease with which finely-divided particulate matter (India ink) could be carried by phagocytic cells from the peritoneum to the pleura via the dia-phragmatic plexus of lymphatic channels. Their work was an outstanding achievement in that it removed from the realm of the mysterious, the phenomenon of hydrothorax occurring as a direct result of fluid within the peritoneal cavity.

The patient, a married woman, aged forty-three years, came to the clinic on November 10, 1943, with a history of having noted a feeling of something present in the lower part of the abdomen in the autumn of 1942. She was able to feel a mass in the right suprapubic region which did not cause any pain but since then it had become larger gradually with much enlargement of the abdomen during the last year. A roentgenogram of the thorax showed that there was fluid in both pleural cavities. Pleural fluid had been aspirated on three different occasions elsewhere. The patient had had few general symptoms except for some dyspnea which was always relieved by the tapping. She had not had any pain, weakness or loss of appetite and her weight had remained the same. Examinations of the blood and urine gave practically normal results. Aside from severe perineal lacerations following the birth of her child, the results of examination were essentially negative. A preoperative diagnosis was a large ovarian tumor—fibroma (?) with ascites and right hydrothorax (Meigs' syndrome); also a rectovaginal fistula.

Right thoracentesis was done on November 13, 1943, and two days later, operation was performed through a low midline incision. A fibroma, 15 by 20 by 15 cm. and weighing 1,370 Gm., arising from the left ovary, was found. A considerable amount of ascitic fluid was removed from the abdomen and left salpingo-oophorectomy was performed. The right tube and ovary were apparently normal and were preserved. The uterus was negative. The patient had a satisfactory convalescence and was dismissed from our care on December 2, 1943.

While there is no doubt that it is an interesting finding when present, yet in the great majority of cases of fibroma there is no evidence of fluid in the thorax. However, in many cases in which there are an abdominal tumor and fluid in the thorax but in which the patient otherwise is in good general condition, the possibility of this syndrome must be considered and the patient should be given the advantage of an exploration.

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THE EFFECT OF PREGNANCY ON BLOOD PRESSURE IN NORMOTENSIVE AND HYPERTENSIVE DOGS*

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(From the Cardiovascular Department, Michael Reese Hospital)

AN IMPORTANT criterion of normal pregnancy in the human being is the blood pressure level. It is therefore not surprising to find a great deal of data assembled on the blood pressure levels in normal pregnant women. While the data are sufficiently clear to lead to the general deduction that the normal pregnant female does not show blood pressure levels outside the normal range and that the changes which do occur are slight, a survey of the literature, excellently summarized by Jensen¹ and Henry,² shows that beyond this the findings are not entirely in accord. There are several reasons for this: (a) The differences in the methods and the criteria used in determining the blood pressure levels, (b) the possible inclusion of pre-eclamptic patients, especially those with "subclinical" forms of pre-eclampsia, and (c) the reliance, in many studies, on statistical data from scattered observations on large numbers of women.

In the few studies in which patients have been followed through pregnancy and the puerperium, the results are more consistent. Thus a number of workers, Strassmann,³ Hare and Karn,⁴ Landt and Benjamin,⁵ Cohen and Thomson⁶ and Hamilton and Thomson,⁷ reported the frequent occurrence of a fall in blood pressure from the fourth to the ninth lunar month. They concur that the blood pressure tends to rise again in the tenth month and that the blood pressure usually reaches the normal level in the first week of the puerperium.

Recently, observations have also been made on the effect of pregnancy on the blood pressure in animals. The data in the normotensive animals are not in agreement.

Thus, Corbit⁸ noted a drop in blood pressure in the normotensive pregnant rabbit before term, Page and Ogden⁹ and Page, Patton and Ogden¹⁰ noted a drop in blood pressure during pregnancy in the rat, while Foa, Foa and Peet¹¹ reported no change. "Pseudopregnancy" in the rat, according to Page, Patton and Ogden,¹⁰ also led to a blood pressure drop. All investigators report a blood pressure drop late in pregnancy in the hypertensive animal, viz., in the rat (Harrison, Grollman, and Williams,¹² Grollman, Harrison and Williams,¹³ Foa, Foa and Peet,¹¹ in the rabbit (Corbit⁸), and in the dog (Goldblatt, Kahn and Hanzal,¹⁴ Mason, Harrison and Blalock¹⁵ and I. H. Page¹⁶).

In the course of the past 6 years we have had occasion to measure blood pressures for varying periods on several hundred dogs. Amongst them there were 31 pregnancies in which blood pressure readings were

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†Serving as Lieutenant, U. S. Army Air Force.

obtained during a portion or all of the pregnancy. Thirteen of these pregnancies were in animals with nephrogenic hypertension and 18 were in normotensive animals. All pregnant hypertensives were observed during the entire period of pregnancy. In the normotensive animals this was possible only in six pregnancies, the other 12 animals being pregnant for various periods on arrival at the laboratory.

We have analyzed and integrated the data in an attempt to gain a better insight of the hemodynamic factors which interplay during pregnancy.

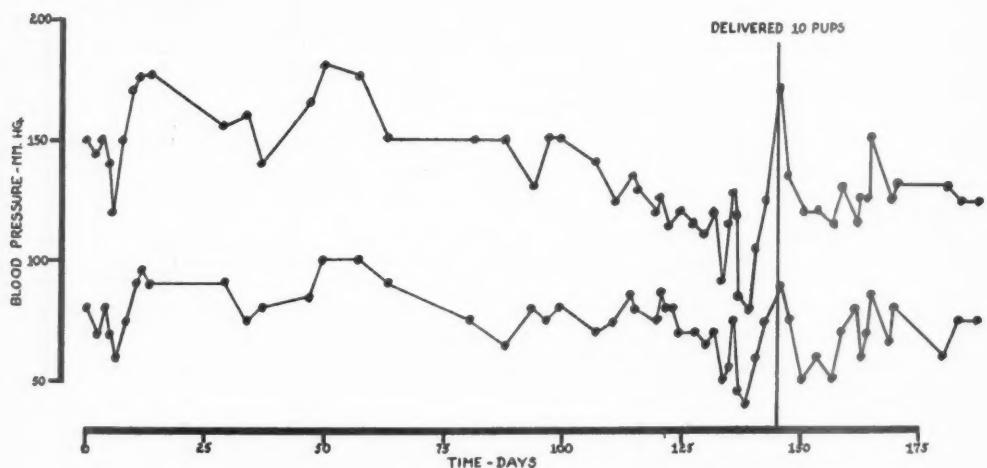


Fig. 1.—Blood pressure changes in pregnancy and in the puerperium in a normal unoperated dog. Systolic pressure above, diastolic below. Discussed in text.

Methods

Blood pressures and heart rates were obtained one or more times weekly with the Hamilton needle manometer¹⁷ in the manner previously described.¹⁸ In this way accurate photographic records for measurements of both systolic and diastolic pressures were obtained on trained unanesthetized dogs. As the animals approached term, daily pressures were taken in some. Hypertension was induced by partial constriction of one or both renal arteries either with the Goldblatt clamp¹⁹ or with linen ligatures.²⁰ In one uninephrectomized dog, hypertension was induced by constriction of the renal vein. Blood N.P.N. observations were made by the method of Koch.²¹ Records were kept of the behavior and reaction to handling of the animals. Conception was assumed to have occurred 60 days prior to term.

Results

Data of pregnancy in a normotensive dog are shown in Fig. 1, and in two hypertensive dogs with two and three pregnancies, respectively, in Figs. 2 and 3.*

(a) *Normotensive Dogs.*—Observations on the blood pressure of the pregnant normotensive dogs, as far as we are aware, have not previously been reported.

*We had occasion to observe two successive pregnancies and three successive pregnancies in two other dogs.

Fig. 1 shows clearly that the blood pressure in this normotensive dog falls as the animal approaches term and that the level returns gradually to its control value early during the puerperium. This dog delivered 10 viable pups. The fall was particularly striking in this animal, reaching a level of 80/40 mm. Hg as compared with the pre-existing control of about 160/80. The heart rate showed a definite acceleration at

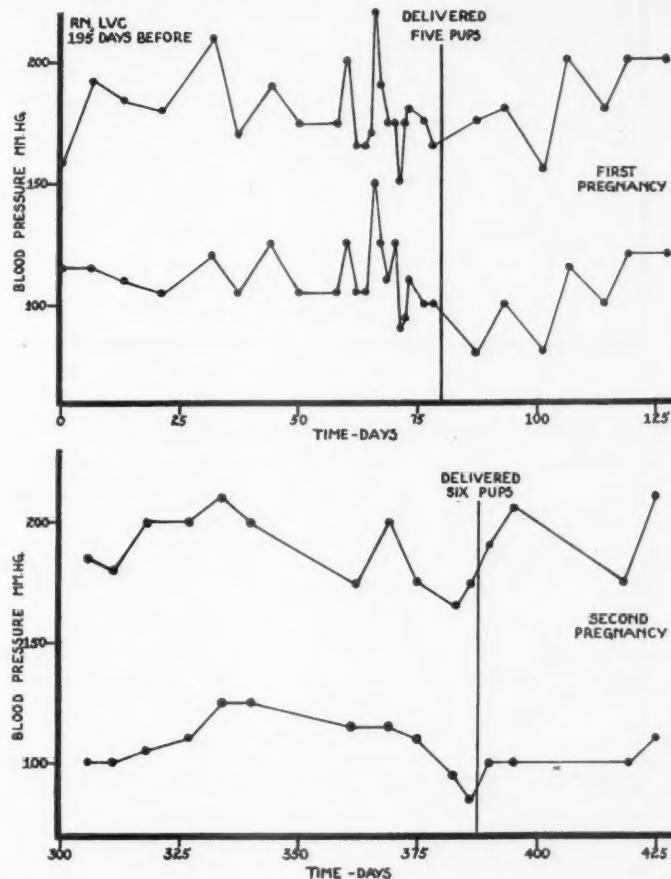


Fig. 2.—Blood pressure changes in two pregnancies in a nephrogenic hypertensive dog. R.N. indicates right nephrectomy, L.V.C., left renal vein constriction. Discussed in text.

the same time. The possibility that this extremely low blood pressure was due to compression of the artery above the point where the femoral artery pressure was obtained while the animal was on its side was ruled out by observing a similar pressure level when the animal was standing.* The second normotensive unoperated dog observed during pregnancy showed no pressure drop; this dog delivered only two pups. Two other normotensive animals with renal artery constriction but without hypertension showed no blood pressure drop. A third dog with three recorded pregnancies showed a diastolic pressure drop of 15 mm. Hg before term in its second pregnancy, and no drop in the

*After the puerperium, bilateral renal artery constriction in this dog led to a marked hypertension and uremia, the animal dying with severe pulmonary edema. At necropsy, a very recent myocardial infarction of the left ventricle was seen, a unique finding in the dog.

third.* Three pups were delivered in each of the three pregnancies without declines in blood pressure, while the one with a slight pressure drop before term delivered eight pups, and the one with the striking fall, ten pups.

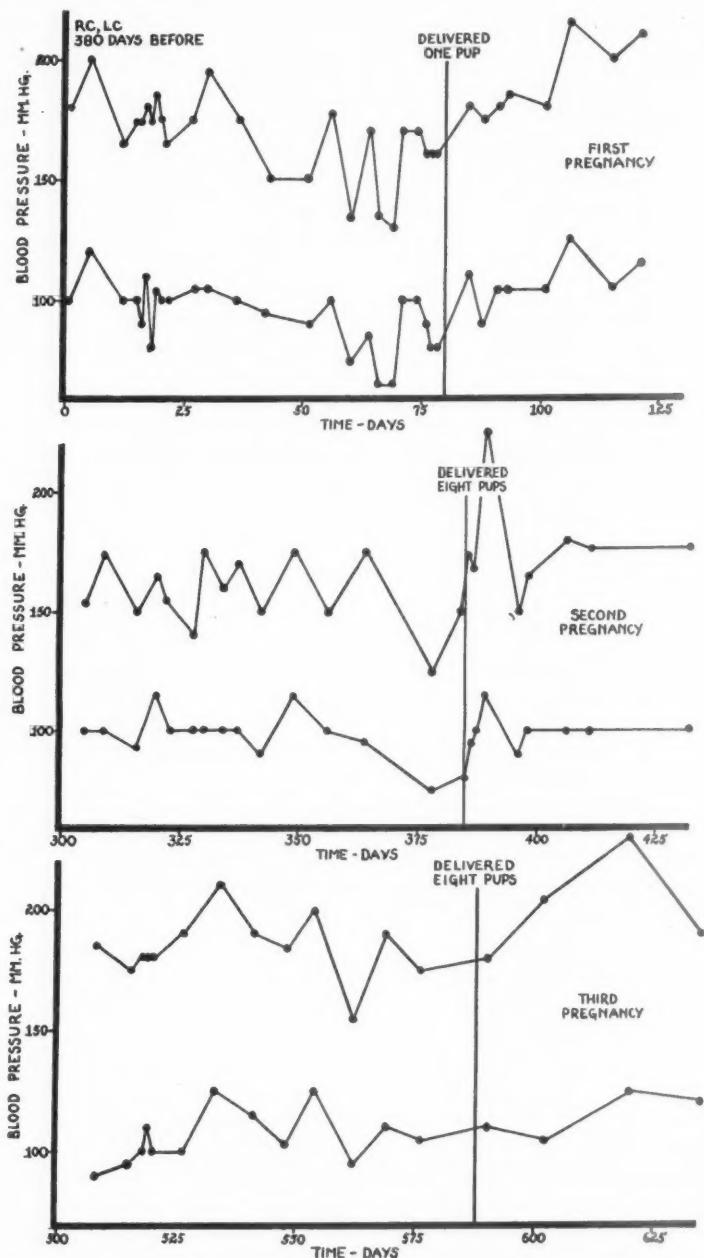


Fig. 3.—Blood pressure changes in three pregnancies in a nephrogenic hypertensive dog. R.C. and L.C. indicate respectively right and left renal artery constriction. Discussed in text.

*The animal arrived in the laboratory late in pregnancy so that the blood pressure data of its first pregnancy were incomplete.

It would thus appear that when the litter is large the blood pressure may fall before term in normotensive dogs. The variability in our results in the dog may explain the apparently contradictory results in other species of animals with normal blood pressure levels. It is interesting to note that in the animal illustrated in Fig. 1 the low blood pressure level, approaching that seen in surgical shock, had no untoward effect on the animal's behavior. This supports the view that the low blood pressure in shock is not the cause of shock but rather is symptomatic, and that such a low blood pressure can occur in circumstances other than shock.

Further indication that pregnancy has a depressor effect on the blood pressure in normotensive dogs was obtained in the twelve dogs coming into the laboratory late in pregnancy. All of these animals failed to show the "excitement hypertension" usually seen in nonpregnant dogs during the period of training.²² It is also interesting to note that during pregnancy most of the animals became docile and quiet. This change in behavior may account for the rise in blood pressure after delivery when the dogs became anxious and excitable and apparently greatly concerned over the welfare of their litters.

(b) *Hypertensive Dogs.*—The results in hypertensive dogs are consistent in showing a drop in blood pressure around term. This occurred in 10 out of 13 hypertensive dogs (e.g., first and second pregnancy of Figs. 2 and 3). However, as these figures show, the time of occurrence of the pressure drop varies from the last third of pregnancy with a return to the pre-existing levels before term (viz., first pregnancy, Fig. 3), to a period at or near term (viz., second pregnancy, Figs. 2 and 3) or early in the puerperium (viz., first pregnancy of Fig. 2). The time of occurrence of this drop is not consistent in repeated pregnancies in the same dog. The absence of the blood pressure drop in two of the exceptions may have been due to the small size of the litter; in one the litter consisted of four pups, and in the other no pups were found, the pregnancy having been terminated by abortion. In the third exception the absence of a blood pressure drop was not due to the small size of the litter.

The drop in pressure caused by pregnancy was not only more consistent but was more marked in the hypertensive than in the normotensive animals. It could not be correlated with the presence or absence of tachycardia or with blood N.P.N. changes.

In three dogs, operations designed to interfere with the renal blood supply were carried out during pregnancy to determine if pregnancy modified the blood pressure response to such operations. In one dog in which this was done, abortion of four stillborn nearly full-term pups occurred four days later. The animal then developed a malignant hypertension and died in uremia six days post partum. In a second dog, there was no effect on blood pressure, two viable pups were born 33 days later following a dog fight in which the mother participated. In the third dog, shown in Fig. 4, the renal vascular operation, which was carried out 38 days before term, led to a definite hypertension which abated temporarily before term. We have previously seen malignant hypertension develop quickly in some nonpregnant dogs and have observed the absence of hypertension following partial renal arterial occlusion in others, and can therefore consider the blood pressure effects in the first two dogs as not peculiar to pregnant animals. This is not the case in the third animal whose data are shown in Fig. 4. The temporary decline in blood pressure in the last part of pregnancy in this dog must have been due to the pregnancy.

Interpretation of Blood Pressure Changes in Pregnancy

Our results on the effect of pregnancy in the renal hypertensive dog are in accord with previous reports described above. Unlike pregnancy in the human hypertensive in which aggravation of the hypertension frequently occurs, pregnancy in the hypertensive animal produces a fall in blood pressure. This effect suggests that experimental forms of hypertension in animals thus far produced are not analogous to many cases of clinical hypertension. Species differences may play a role in this effect.

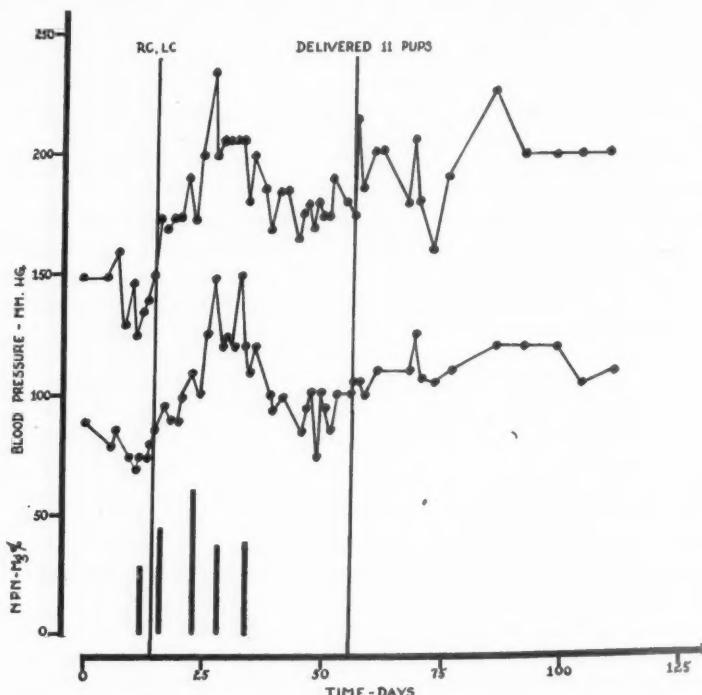


Fig. 4.—Blood pressure changes following interference with renal blood flow during pregnancy. R.C. and L.C. indicate right and left renal artery constriction. Also shown is the blood N.P.N. levels in columns below the blood pressure curves. Discussed in text.

The drop in pressure late in pregnancy or early in the puerperium has been ascribed to some action of the fetal kidneys, overcoming in some fashion the humoral mechanism of renal hypertension of the mother. The fact that we observed a similar fall in the normotensive animal, as did Corbit,⁸ and that "pseudopregnancy" has a similar effect (Page, Patton and Ogden¹⁰) would tend to exclude this mechanism. This view is supported by the report that there is no difference in response to renin between pregnant and nonpregnant animals (Kellar and Sutherland²³).

Other possibilities suggest themselves to account for this pressure drop. The first is the occurrence of a decrease in the peripheral resist-

ance on a mechanical basis beyond the point where homeostatic mechanisms can cope with it. Another possibility is the production of humoral vasodepressor material in large amount either in the placenta or elsewhere as a result of pregnancy. A third possibility is a decrease in the production of humoral vasoconstrictor materials which help to maintain the blood pressure at normotensive levels and presumably operate also in the presence of renal hypertension.

There is no question at present that pregnancy leads to profound changes in the cardiovascular system. The placenta itself represents a large low-resistance shunt²⁴⁻²⁷ which in man may contain up to one-sixth of the blood volume.^{25, 28, 29} The placenta grows rapidly in pregnancy and apparently somewhere about midterm its size becomes sufficient to affect the total systemic peripheral resistance. The rapid continued growth of the uterus after this period continues to increase the size of the shunt through it. In the last lunar month the placenta becomes hyalinized, more compact, and the blood flow through it may decrease by as much as fifty per cent. An increase in resistance also is caused at this time by an increase in uterine tone (Reynolds²⁵).

These changes in the uterus must be integrated with the striking changes in the general circulation which occur simultaneously. These changes in the cardiovascular system reach their maximum in man at about the ninth lunar month and then regress during the tenth lunar month and in the puerperium (Hamilton and Thomson⁷). There is a striking increase in cardiac minute output (up to fifty per cent) and stroke output in man^{6, 27, 30-33} and in the dog,³⁴ in circulating blood volume in man^{6, 27, 35-37} and in velocity of blood flow in man.^{6, 38} The blood viscosity is decreased in man,⁶ the venous pressure falls slightly in man.³⁹ Certain changes in particular organs have been noted, viz., the spleen of the dog shrinks in size,⁴⁰ the flow in the limbs of man is increased⁴¹ but the flow in the kidney of man as determined indirectly by clearance studies does not change.⁴² No evidence of cardiac hypertrophy was obtained in pregnant animals by Van Liere and Sleeth.⁴³

It is apparent from the above analysis that the presence of an ever-increasing low-resistance shunt for the first 90 per cent of pregnancy would tend to decrease the effective total systemic peripheral resistance on a purely mechanical basis and so, by itself, would tend to lead to a drop in arterial blood pressure with its maximum at the time when about 90 per cent of the period of pregnancy was reached. This effect is counterbalanced by the increase in circulating blood volume and cardiac output which would tend to keep the arteries filled and so maintain the blood pressure. The homeostatic function of the nervous system operating primarily to cause vasoconstriction of the splanchnohepatic circuit would assist in this process. Ordinarily these factors manage to keep the blood pressure at its normal level for most of pregnancy but in animals this appears to fail to do so late in pregnancy.

While the foregoing explanation may be adequate to account for the blood pressure drop, it requires the assumption that there is a great variability in the time when the placental shunt effect dominates over that of the increased cardiac output and circulatory blood volume. Further, it fails to account for those experiments in which the blood pressure drop first appears in the puerperium.

It is quite possible that the variability in the time of the blood pressure drop in pregnancy is to be accounted for by some humoral mechanism. Either some of the humoral vasodepressor factors evolved during pregnancy become potent at this time or the usual humoral pressor substances helping to maintain the blood pressure become less effective. Endocrine disturbances accompanying pregnancy may release vaso-dilator substances which might produce the blood pressure changes.

It should be emphasized that despite the marked dynamic alterations which occur in pregnancy, the blood pressure during most of pregnancy is surprisingly little affected. This illustrates anew the normal operation of homeostatic maintenance of blood pressure at a constant level.

Abortion in Pregnant Dogs

Recently, Dill and his associates⁴⁴⁻⁴⁶ have reported on the great frequency of abortion and resorption of fetuses in pregnant rabbits and dogs following operative interference with the renal blood supply. Many of their animals developed signs and symptoms which were interpreted as simulating those of the toxemias of pregnancy seen in the human subject. The pathological changes in the liver and other organs were considered to confirm this view.

Blalock, et al.,⁴⁷ confirmed the great frequency of abortion and fetus resorption in dogs following interference with the renal circulation. However, these authors considered that the lesions found at necropsy did not resemble those seen in the toxemias of pregnancy but rather resembled those associated with severe renal ischemia.

It has been shown by Greene⁴⁸ that spontaneous abortion, associated with characteristic alterations in the liver morphology, occurs in non-operated pregnant rabbits. Furthermore, it is well known that any operation upon pregnant rabbits can readily lead to abortion. For example, we found in a series of nonoperated pregnant rabbits that the simple procedure employed by us to obtain their blood pressure⁴⁹ led in every instance to spontaneous abortion.

Similarly in the dog we found that premature delivery late in pregnancy occurred commonly when dogs were subjected to routine nembutalization and devocalization. One of our normotensive pregnant dogs delivered immediately after participating in a dog fight; the two pups born were viable but died 48 hours later. Furthermore, we had occasion to observe the effect of operative interference during pregnancy in several dogs. One dog, subjected to an extensive chest operation,⁵⁰ aborted seven nonviable almost full-term pups three days

later. Four other of our dogs were subjected to operations on the renal blood vessels during pregnancy. In two dogs, five viable pups were delivered four days later. A third dog delivered three full-term stillborn pups four days after the operation. This dog then developed a malignant hypertension with a blood pressure up to 210/145 mm. Hg

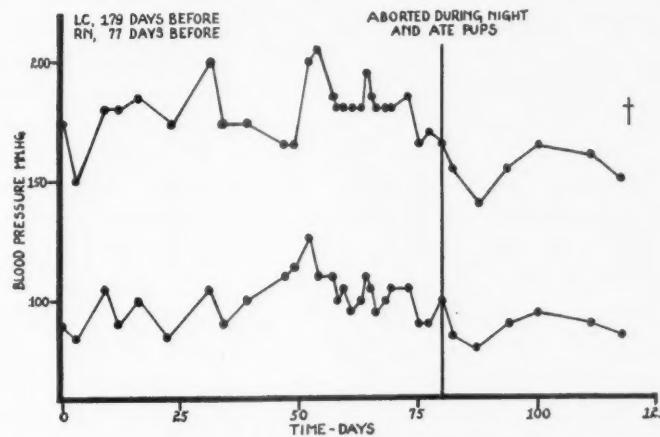


Fig. 5.—Blood pressure changes in an animal with spontaneous abortion. L.C. indicates left renal artery constriction, R.N., right nephrectomy. Discussed in text.

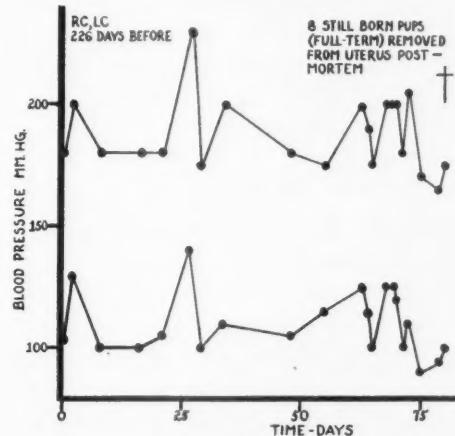


Fig. 6.—Blood pressure changes in an animal with spontaneous abortion. R.C. and L.C. indicate right and left renal artery constriction. Discussed in text.

and uremia and died six days post partum. In a fourth dog (Fig. 4) delivery of 11 full-term viable pups occurred 38 days after surgery, four of the pups dying the same day; the dog survived and maintained the hypertension.

The blood pressure data on two dogs with hypertension which aborted spontaneously are shown in Figs. 5 and 6. The first dog (Fig. 5) was under observation for almost a year, the hypertension was moderate but the diastolic pressure ranged about 15 to 25 mm. Hg above the previous control level. Following a unilateral nephrectomy, the blood N.P.N.

rose to 50 mg. per cent. The dog later became pregnant and showed a slightly elevated blood pressure. The animal then aborted during the night. This was followed by a lowering of the blood pressure level, and the blood pressure rose only slightly in the interval until the dog died 39 days post partum. Before death the legs became progressively weaker until the animal lost the ability to walk about.

The second dog (Fig. 6) was also observed for almost a year. It too had a moderate hypertension, the diastolic blood pressure ranging from 15 to 50 mm. Hg above the control level found before the renal operation, but there was no evidence of uremia. Just before term the blood pressure fell and the heart rate increased. The dog developed convulsions whenever disturbed, became comatose and died. The blood N.P.N. five days before death was normal. At autopsy eight full-term stillborn pups were removed from the uterus. The liver was found to be very small, hard and yellow, suggesting yellow atrophy. Histologically, it showed cloudy swelling and central fatty degeneration with necrosis. The changes in the liver were considered by Dr. O. Saphir of the Pathology Department to be compatible with a severe toxic condition as found in a general toxemia, septicemia or a virus disease.

Our experience with these animals leads us to conclude that operations late in pregnancy, whether leading to malignant hypertension, to benign hypertension or to no change in blood pressure, will increase the susceptibility to abortion in the dog. Abortion occasionally occurs spontaneously in normotensive and hypertensive animals, but further studies will be required before the relation of such abortion to the toxemias of pregnancy is understood.

Summary

1. The blood pressure in normotensive and especially in hypertensive dogs tends to fall late in pregnancy. The degree of reduction of blood pressure is apparently affected by the size of the litter.

2. It is possible that the blood pressure decline is related to the low-resistance placental circuit which develops during pregnancy. It is also possible that some humoral factor (not involving the fetal kidneys) caused by the maternal endocrine alterations which accompany pregnancy contributes to the blood pressure change and helps to account for the variability in the time at which this blood pressure drop occurs.

3. Surgical or other traumatic intervention during the latter part of pregnancy appears to predispose to abortion in the dog.

We are grateful to the members of the department for help in obtaining the data used and to Miss Louise Friedberg for her suggestions in preparing this report.

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TRANSPLANTATION OF ABDOMINAL FASCIA FOR THE RELIEF OF URINARY STRESS INCONTINENCE*

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LOSS of control of urination under muscular effort, such as coughing, sneezing, walking, etc., is a complaint commonly encountered among gynecologic patients. This symptom, termed stress incontinence, often arises following the production of injuries to the supports of the bladder and urethra during the course of parturition, in women who have been previously normal. Less frequently, it is observed in female children with no obvious anatomic defect. They may outgrow it, or it may persist into adult life. The cause of incontinence in such young nulliparous individuals must be ascribed to a faulty development of the poorly understood mechanism which controls the retention of urine in, and the emptying of, the bladder. The occurrence of child-birth in this last group is very apt to greatly aggravate this symptom by superimposing injuries to the supports of the bladder and urethra.

While the more or less standardized gynecologic operations, based on the repair of the supporting structures of the bladder and upper urethra and upon tightening the vesicle sphincters, give excellent results in the relief of this symptom in the majority of instances, most observers report an incidence of failure in from 10 to 20 per cent. Often subsequent operative procedures of a different type may fail to relieve the patient. Failures are particularly likely to occur in individuals whose childhood history suggests a lack of development of the mechanism of urinary control. These patients, unhappy enough before operation, become unhappier and more unfortunate following one or more operative failures.

In March, 1942, Aldridge¹ described an operative technique for the relief of intractable urinary stress incontinence by the use of strips of the abdominal fascia drawn through the rectus muscles and united to form a sling under the bladder neck. This was carried out after well-recognized procedures had been utilized to repair the supports of the urethra and bladder in the preliminary phase of the operation. This technique had been put into practice in the treatment of a fifty-one-year-old woman in whom three previous operations had failed to relieve a marked stress incontinence which had been existent for twenty-nine years. Complete relief of symptoms followed this operation.

This favorable result called to mind several patients in the follow-up clinic of the gynecologic service of Bellevue Hospital, in whom re-

*Read at a meeting of the New York Obstetrical Society, December 14, 1943.

peated operative procedures of varying types had failed to relieve this distressing symptom. These miserable patients were continuously begging for further surgery, always hoping that one more attempt would produce a favorable result. It was determined to attempt the application of this method in a final effort to improve their control of urination.

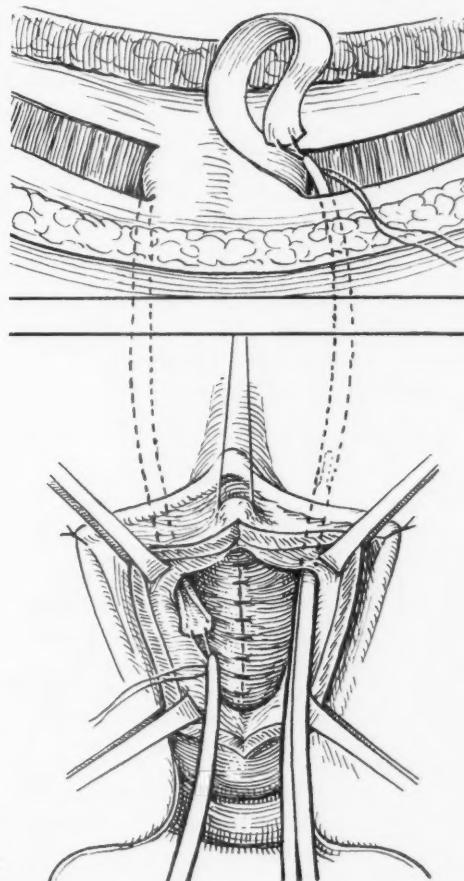


Fig. 1.—The fascial supports of the bladder and upper urethra have been plicated. Through a large curve transverse incision, the center of which lies about 2 cm. above the symphysis, two strips of fascia 7 to 8 cm. long and 2 cm. wide have been freed. Their inner attached ends lie about 1.5 to 2 cm. from the midline. Through their tips have been passed mattress sutures. On the left a uterine forceps has been passed upward between the fascia and the pubic ramus, through the prevesicle space and the rectus muscle. It is grasping the mattress suture. On the right, the fascial strip has been drawn through by means of the mattress suture in the reverse direction to which the clamp was passed.

The technique utilized was almost exactly that described by Aldridge. In only one particular was a departure made from the original procedure. In the first case on which it was attempted, it was found to be impossible to secure fascial strips of sufficient length in order to overlap and suture their ends in the formation of the sling. Therefore, mattress sutures were passed through the ends of the strips, the ends of the sutures then being drawn through the rectus muscles, past

the lateral aspect of the bladder neck, and out of the vaginal incision by a uterine dressing forceps (Fig. 1). By means of these sutures the fascial strips could easily be drawn along the same course. The strips were approximated to form a sling under the bladder neck by simply tying the sutures together (Fig. 2). The bladder neck became elevated and brought forward, close to the symphysis, when this was done. It is believed that this modification simplifies and makes easier the original technique. It was carried out in all four of the patients included in this report. Except for this departure, the reader may be referred to Aldridge's¹ excellent description and illustrations for the technical details.

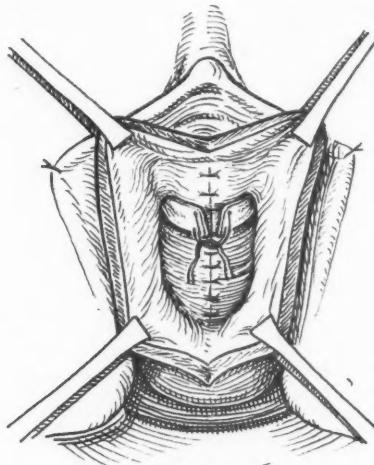


Fig. 2.—The fascial strips are being approximated to form a sling by tying the mattress sutures together. This sling should be fairly tight, and should retract the bladder neck upward and forward behind the symphysis. Actually, at the operation the bladder neck disappears so that the lower border of the sling cannot be seen as depicted by the artist.

In all, four patients have been operated upon, plastic procedures of varying extent having been carried out as indicated in the individual case. Following this, fascial strips transplanted from the abdominal wall, have been utilized to form a sling to support the bladder neck. The individual reports of these patients follow in some detail in order to demonstrate the magnitude of the gynecologic problem and because in one of those patients a most unusual complication arose.

CASE 1.—(No. 8523-43.) Mrs. J. V., 38, para iii, gravida iv, was admitted to the gynecologic service, Bellevue Hospital, on February 20, 1943, for the fifth time, with a chief complaint of stress incontinence. In her first pregnancy in 1924, she was delivered by forceps at home after a labor of five days. Her symptoms date from this event. Full-term pregnancies occurred in 1927 and 1933, and a three-month spontaneous abortion in 1935. Her record showed that she had been admitted in 1930 with the same complaint. At this time a diagnosis of cystocele, relaxed vesicle sphincter and relaxed perineum were made. The cystocele was repaired, the Kelly technique was employed to tighten

the vesicle sphincter, and a perineorrhaphy was performed. No improvement in the incontinence occurred. In 1935, a second attempt to control the symptom was made, utilizing the same procedure except that perineorrhaphy was found to be unnecessary. Again complete failure was the result. In 1940, a third attempt was made utilizing the technique described by Kennedy.² No relief was obtained. Six months later, in the same year, a fourth attempt was made to help her by the implantation of a strip of fascia lata under the bladder neck. No noticeable improvement followed.

Physical examination showed a short, stocky, obese woman of healthy appearance. General examination contributed no relevant findings. On pelvic examination, she was found to have excellent support. The anterior vaginal wall was very slightly relaxed. The cervix was posterior, normal in appearance. The corpus was anterior, normal in size and freely movable. The adnexa were negative. There was no loss of uterine support. The general impression of the examiner was that an excellent result had been attained by the previous operative procedures. Nevertheless, on the slightest straining the patient could eject a stream of urine for several feet. Her blood pressure was 120/70; urine examination negative; blood count normal.

On March 5, 1943 she was operated upon, the first step consisting of a wide dissection of the vesicle and urethral fascias. The fascial plane adjacent to the bladder neck was followed upward until the prevesicle space was entered. The fascias were then united in the midline and plicated beneath the bladder and upper urethra. The incision in the anterior vaginal mucous membrane was left open. The patient was then put in the dorsal position and a large transverse incision was made down to the fascia, curving upward on each side of the midline, its center being about 2 cm. above the symphysis. The fascia was cleared of fat and strips 7 cm. long by 2 cm. wide were freed on each side from the external oblique and rectus muscles. The medial attachment of each strip was carefully preserved about 1½ to 2 cm. from the midline. The outer two-thirds of the fascial defect thus created were immediately repaired with running catgut sutures. The patient was then returned to a lithotomy position and an attempt was made to pass a curved clamp through the vaginal incision along the fascial plane lateral to the bladder neck, through the prevesicle space, and rectus muscle in order to grasp the fascial strip and pull it through in the reverse direction. It was then discovered that no clamp long enough to accomplish this purpose was available. A uterine packing forceps was employed but the strips slipped out of the closed blades on very gentle traction. Finally mattress sutures were placed in the tip of each fascial strip and these were drawn through on each side of the bladder neck. Again difficulty was encountered in pulling down the strips so that they could be overlapped and sutured to form a sling. This was finally accomplished by simply tying the sutures together. This resulted in a marked elevation of the bladder neck. The vaginal mucosa was then closed, and at the same time the remainder of the fascial defect in the abdominal wall was approximated. Eight to ten grams of powdered sulfanilamide were dusted in the abdominal fat, and the skin was closed by interrupted sutures, a small rubber tissue drain being left at each angle. A mushroom catheter was placed in the bladder.

Her postoperative course was uneventful. Moderate serosanguineous discharge was noted from the abdominal wound. The drains were re-

moved on the third day, the incision healing without infection. The retention catheter was accidentally removed on the fourth day and was not replaced because it was found that the patient voided spontaneously. She was kept in bed three weeks. Pelvic examination before discharge showed the vaginal incision healed, the urethra being held tightly against the back of the symphysis. She had perfect control of urination.

This patient has been seen on several occasions since her discharge, the last time being in September, 1943. She is completely relieved of urinary incontinence even when undertaking violent exercises. No weakness is evident in the abdominal wall.

CASE 2.—(No. 22741-43.) Mrs. S. F., aged 42, white, married, para ii, gravida ii, was admitted to the gynecologic service, Bellevue Hospital, for the second time on May 11, 1943, complaining of marked stress incontinence. Her two children, born in 1932 and 1934, had both weighed over 9 pounds at birth. Loss of bladder control was noticeable after the second pregnancy but became much worse in 1940. Her previous admission in April, 1942, had been for the same complaint. At this time a cystocele was repaired, the bladder neck and urethra being plicated following the Kennedy² technique. A perineorrhaphy was performed. No relief had followed this procedure. Her menstrual history was normal; her blood pressure was 170/105; the laboratory data were irrelevant.

Except for the blood pressure findings, her general physical examination proved normal. The abdominal examination was negative. On pelvic examination, she was found to have adequate perineal support; moderate relaxation of the lower half of the anterior vaginal wall was noted; the cervix was posterior, flush with the vaginal vault; the corpus uteri was anterior and not enlarged; the adnexa seemed normal.

On May 15, 1943, she was operated upon, the identical procedure being used that has already been described in Case 1. On this occasion the fascial strips were drawn down on each side of the bladder neck by mattress sutures passed through their tips, by preference and not in desperation. The strips were united under the bladder neck by tying the sutures together. A median episiotomy had to be performed in order to gain proper exposure, and this was closed at the conclusion of the main operative procedure.

This patient had an uneventful postoperative course. She voided spontaneously and never required catheterization. She was examined on the seventeenth postoperative day, just before discharge, at which time the vaginal and abdominal incisions were found to be healed by primary union. The bladder neck was well supported and the urethra held snugly against the back of the symphysis. She had perfect control of urination.

She has been seen several times since discharge, the last occasion being on December 6, 1943, and reports that she is absolutely free of symptoms except that she is aware of slight suprapubic tugging when she coughs. No weakness of the abdominal wall is present. Pelvic examination shows an excellent anatomic result.

CASE 3.—(No. 22794-43). Mrs. S. T., aged 51, a married, white female, para iii, gravida v, was admitted to the gynecologic service, Bellevue Hospital, on May 11, 1943, for the fourth time complaining of stress incontinence, urgency of urination and the protrusion of a mass

from the vagina. Her children had been born without difficulty in 1907, 1917, and 1919, their weights at birth being unknown. She had had two spontaneous miscarriages. In 1926 she had had a left nephrectomy for chronic suppurative nephritis. In 1928 she underwent cholecystectomy. About 1935, at the age of forty-three, the onset of hypertension was noted and between 1938 and 1941 she was treated with digitalis for mild heart failure.

On the occasions of her first admission in April, 1938, she complained of frequency of urination of five to six years' duration and of stress incontinence for the preceding eighteen months. She was found to have a large cystocele, a relaxed perineum and multiple fibroids. At her operation, the cystocele was repaired, a Kelly stitch being utilized to tighten the vesicle sphincter. A perineorrhaphy was performed, following which a supravaginal hysterectomy was carried out.

Following this admission, her cystocele recurred very rapidly and she had no relief from her urinary symptoms. She was readmitted in January, 1939, when the cystocele was once more repaired, the bladder neck and upper urethra being plicated according to the Kennedy² technique. In May, 1941, because of failure to relieve her symptoms and the second recurrence of cystocele, she was readmitted. The cystocele was again repaired and an attempt was made to interpose the cervical stump beneath the base of the bladder. This operation proved equally unsuccessful.

Physical examination revealed an obese elderly female. The heart was clinically enlarged and a systolic murmur could be heard over the entire precordium. The rhythm and rate were normal and no suggestion was present of cardiac decompensation. Abdominal examination revealed scars in the upper right quadrant, in the left flank and in the suprapubic region. On pelvic examination, there was found a large cystocele with partial prolapse of the cervical stump and vaginal vault. A rather advanced degree of atrophy was noted. Her blood pressure was 240/110. The laboratory findings revealed nothing noteworthy.

She was operated upon May 13, 1943. At this time the cystocele was again repaired, the broad ligaments were approximated in the midline following the excision of the cervical stump, and the fascial supports of the posterior vaginal wall were dissected out and approximated. The extensive vaginal incision was then closed except for the anterior wall and the operation was concluded by the transplantation of fascial strips from the abdominal wall according to the previously described method. The anterior vaginal wall was then closed and the vagina was packed with plain gauze. This extensive procedure took over two hours to perform.

Immediately following the operation the patient showed a moderate degree of shock. Her blood pressure was 105/65, her pulse 50, and her color poor. She was given a transfusion of 500 c.c. of bank blood, and later an infusion of 1,000 c.c. of 5 per cent glucose in saline. She rapidly responded to this, appearing much better the next morning with a blood pressure of 160/90, a pulse of 75, and a temperature of 99° F. Because of frequent vomiting, she was given 1,000 c.c. of 5 per cent glucose in saline. However, it was noted at this time that her urinary output had markedly decreased. Catheterization on the evening of her operation yielded 200 c.c.; at 5:30 A.M., on the first postoperative day, 90 c.c. This trend rapidly increased, only 20 c.c. being obtained at 7 P.M., an additional 20 c.c. being voided at midnight. On the second

day postoperative, May 15, no urine could be obtained on repeated catheterizations. The patient continued to vomit and was given several infusions. Because the onset of this condition was gradual, some urine being excreted into the bladder during the first thirty-six hours after operation, it was felt that the left ureter must be occluded by edema rather than ligated. The possibility of anuria due to transfusion was considered but no evidence of hemolysis could be found. This situation was made even more serious because the patient had only one kidney, her right, the left having been removed in 1926. An intravenous pyelogram was obtained and no dye could be visualized in the right kidney pelvis or ureter. A blood chemistry showed a nonprotein nitrogen of 33 mg. per cent. It was decided that the patient should be observed a little longer in the hope that the edema would subside. On May 16, the third postoperative day, no urine could be found in the bladder on catheterization. Her nonprotein nitrogen was reported as 43 mg. per cent. She was subjected to cystoscopy at which time the right ureteral orifice was visualized with difficulty because the floor of the bladder was elevated by its new fascial support. Fairly marked edema was present about the right ureteral orifice and attempts to introduce catheters and bougies resulted in failure. On May 17, the fourth postoperative day, no urine was found in the bladder. The nonprotein nitrogen had risen to 75 mg. per cent. The patient was stuporous and showed pallor and rather a marked edema.

It was felt by both the urologic and gynecologic departments that radical steps must be taken in order to prevent catastrophe. The choice lay between the removal of all sutures in the operative area for the relief of the evident edema, or drainage of the right kidney until the edema began to subside. The hazard of the former procedure lay in the fact that sutures could not be replaced without risking a recurrence of the edema, making the probability of a tremendous postoperative pelvic hernia almost certain. The latter course was therefore decided upon.

The patient was taken to the operating room and the right kidney was exposed. A double ureter was found, both the ureters and the kidney pelvis being markedly distended and tense. The ureter was aspirated and urine was obtained under pressure. A moderate-sized nephrostomy tube was inserted through the kidney parenchyma and urine immediately began to drain. The wound was closed after sprinkling sulfathiazole powder between its layers. The patient was returned to the ward in good condition.

In the next six hours 700 c.c. of urine passed through the tube. Immediate improvement followed. She began to take fluids well and this was supplemented by 2,500 to 3,000 c.c. of fluids by infusion daily. Her nonprotein nitrogen dropped to normal levels. By May 20 (seven days postoperative, gynecologically; three days postoperative, urologically) her condition was excellent. On May 21, exactly eight days after the primary operation, she began to pass urine in small amounts from the bladder. On May 25, she passed 325 c.c. in a twelve-hour period; during this same period the drainage from the nephrostomy tube gradually diminished. On June 1, fifteen days after the nephrostomy, she developed a fever of 103° F. due to a urinary infection, but this rapidly cleared up under mandelic acid therapy. On June 13, twenty-seven days after the nephrostomy and thirty-one days after the primary procedure, the nephrostomy tube fell out and was not replaced. This

wound rapidly closed. She was examined just before discharge, at which time the abdominal, vaginal and nephrostomy incisions were found to be well healed. Excellent pelvic support was present, the vaginal vault being held at a high level, the bladder well supported, and the urethra fixed snugly against the back of the symphysis. Intravenous pyelography done before discharge showed moderate dilatation of the right ureter and kidney pelvis.

The patient has been seen on several occasions, the last time being December 4, 1943, and shows an excellent anatomical result with no evidence of recurrence of her former lesions. She has perfect control of urination. Her only complaint consists of occasional slight pain in the region of the right kidney. Intravenous pyelograms have shown a slight persistent dilatation of the right ureter and kidney pelvis.

Encouraged by these results on patients not cured by one or more previous operations, the question as to whether this procedure might be utilized as a primary measure in the treatment of stress incontinence arose. Certainly it could be strongly considered as a primary procedure if the chance of cure by other operations appeared questionable or unlikely. Fortunately, such a case presented herself shortly after these patients had been treated and observed.

CASE 4.—Mrs. M. T., aged 45, married, white, para ii, gravida iii, presented herself, complaining of leakage of urine on coughing, sneezing and walking, which had been present to an almost disabling extent for ten years. Since earliest childhood she had suffered from defective control of urination but this had become much more pronounced after the birth of her children, now twelve and sixteen years old. At present she was only completely continent on sitting and lying down. On walking, she immediately began to dribble urine and this became more pronounced on the slightest exertion. She constantly wore a cotton pad to protect herself. Her general health was excellent and she had had no previous operation. Her menstrual history was normal.

Physical examination showed a short, obese woman who appeared in excellent health. General examination revealed no significant findings. On pelvic examination, she showed a moderate cystocele, a relaxed perineum and a moderate degree of rectocele. A Bartholin cyst was present in the right labium. The cervix was posterior, well supported and normal in appearance. The corpus uteri was anterior and not enlarged. The adnexa were normal. Blood pressure was 120/70. The laboratory findings were irrelevant.

This patient (716,559) was admitted to the Sloane Hospital on August 4, 1943, and operated on the following day. The procedure already outlined in Case 1 was carried out, following which the right Bartholin cyst was excised, the rectocele was repaired, and a perineorrhaphy was performed.

Her first postoperative day was marked by a rise in temperature to 102° F., but thereafter her course was practically afebrile. Catheterization at regular intervals was employed until August 17 (the twelfth postoperative day) because of inability to void. During this time sulfanilamide 0.5 Gm. was given three times a day to prevent cystitis. During the next five days she complained of urgency and frequency. She was examined on the day of discharge, August 23, at which time the abdominal and vaginal incisions appeared well healed. The urethra

was tight against the back of the symphysis, the bladder neck being high and well supported. Her perineum showed an excellent postoperative result.

She has been seen on several occasions since leaving the hospital. At the last visit on December 8, 1943, she stated that for the first time in her life she had complete control of urination. She was able to undergo all kinds of exertion with no evidence of leakage, usually voiding voluntarily without urgency at three- to four-hour intervals.

Little comment need be added to the details contained in the outlines of these four cases. In the opinion of the writer, the outlook for improvement or cure in all four cases was dubious had they been treated solely by the usual gynecologic procedures. The value of using transplanted fascial strips from the abdominal wall in addition to such procedures is demonstrated amply by the fact that all four patients show a perfect symptomatic result. It may be said that the follow-up on these patients is too short. That cannot be avoided since they have all been cared for during the past year. Observation will be continued with high hopes that the early results will be permanent.

Summary and Conclusions

1. Fascial strips from the abdominal wall have been utilized to form a sling under the bladder neck after the performance of procedures designed to improve the support of the bladder and upper urethra.
2. Three patients, with a chief complaint of urinary incontinence, totaling between them eight operative failures with a variety of methods, have achieved perfect symptomatic and anatomic results by means of this procedure.
3. One patient, whose background of poor urinary control in childhood suggested difficulty in the operative correction of incontinence, has apparently been cured.
4. The occurrence of an interesting complication has been described and its treatment outlined.
5. The operative technique of this procedure, originally proposed by Aldridge, has been slightly modified and, it is to be hoped, simplified and improved.
6. Additional evidence is presented that this procedure is of the greatest value when other methods have failed. Further, it is suggested that the operation may be used as a primary procedure when study of the patient suggests that the usual operations have a strong possibility of failure.

NOTE:

CASE 1.—Mrs. J. V. (No. 8523-43), Bellevue Hospital, returned for a follow-up visit on December 15, 1943, the day after the above report was presented. She stated that, with the return of cold weather, she had noted slight incontinence on going out of doors. This also occurred when she lost her temper with her children. On violent coughing, she also lost a few drops of urine. She felt quite

satisfied, however, with the marked improvement since her operation and showed no desire for further surgery. Examination showed a well-healed abdominal incision with no evidence of hernia. Pelvic examination showed an excellent post-operative result, the bladder being firmly fixed high up and close to the neck of the symphysis.

References

1. Aldridge, A. H.: AM. J. OBST. & GYNEC. 44: 398, 1942.
2. Kennedy, W. T.: AM. J. OBST. & GYNEC. 34: 576, 1937.

Discussion

DR. GEORGE W. SLAUGHTER.—The fact that a serious complication occurred in one case should in no way detract from the usefulness of the operation. Temporary unilateral anuria, I believe, is probably a frequent transient complication in many gynecologic operations due to edema of involved tissues with resultant pressure on a ureter. Unless, as in this case, there is only one functioning kidney, the condition is never noted and spontaneous recovery results as soon as the edema subsides. Apparently no damage ensues as long as the involved kidney remains uninfected.

As Dr. Studdiford has pointed out, three possible methods of attacking this problem were at hand. First, a ureteral catheter might be passed to the kidney. This was attempted, but because of angulation a catheter could not be introduced into the ureter. Protracted attempts might easily have resulted in additional edema.

The second procedure, the removal of the sutures, would certainly have destroyed part, if not all that the operation was to gain, with no certainty that extrinsic pressure on the ureter would be relieved.

The third method, a nephrostomy, although it would necessitate subjecting the patient to a second operation, would surely bear fruit. My opinion was that this was the better choice, since it is one of the simplest of all renal operations and can be performed in about twenty minutes. There was every indication in this case that the ureter was being compressed by edema, rather than that it had been ligated, as evidenced by the gradual diminution of the urinary output rather than a sudden stoppage. Nephrostomy would, however, have in any case been the next step, even though the ureter never again became patent.

DR. ALBERT H. ALDRIDGE.—Progress in the development of surgical techniques to cure urinary incontinence by transplantation of muscles and fascia dates back to about 1900. For this purpose at least seven different muscles have been transplanted either alone or in combination with strips of fascia.

A matter of importance is how well transplanted fascia will stand the test of time. The patient reported when the technique used by Dr. Studdiford was first described is now two and one-half years from operation and is still free of symptoms. In the meantime I have used this technique in four additional cases. Details regarding these cases will be reported later. Briefly, it may be stated that results in two of the four cases appear to be entirely satisfactory. A third seems to have a good result from the mechanical standpoint but has slight difficulty at times, probably from bladder irritation due to a persistent urinary tract infection. The infection started following a previous vaginal plastic operation for the same condition, was present at the time of her last operation and has not been entirely eliminated by subsequent treatment. When the urinary infection is kept under control with treatments, she is entirely continent for long periods of time. The fourth patient in whom this technique was used is emotionally unstable and has been under the care of a psychiatrist. When she fails to sleep well or is unusually disturbed emotionally, she occasionally loses a small amount of urine on

getting out of bed in the morning. Otherwise, she is entirely free of bladder symptoms and obviously has no real stress incontinence of urine at any time.

Experience has proved the importance of certain points in the management of these cases. Urinary tract infections should be eliminated as completely as possible before undertaking to relieve urinary incontinence by surgical means. In general, fascial transplantation to relieve urinary incontinence should be used only for patients in whom vaginal plastic operations have failed. It should always be used in conjunction with the usual vaginal plastic procedures for incontinence and should never be regarded as a substitute for them.

I have found a pelvimeter to be helpful in determining the length of fascial strips to be transplanted. With one tip of the pelvimeter placed at the proximal end of the urethra in the vagina, and the other on the abdominal wall, it is not difficult to estimate the length of strips that will be needed to form a fascial sling beneath the urethra.

Dr. Studdiford has recommended the use of mattress sutures in the distal ends of the fascial strips to facilitate drawing them backward into the vaginal wound. I have used this same procedure and have found it helpful.

Dr. Studdiford has apparently also gotten satisfactory results by tying the mattress sutures in the ends of the fascial strips together beneath the urethra instead of overlapping the distal ends of the strips and fixing them together by additional sutures. Success with this technique must depend upon a permanent fascial sling beneath the urethra. For this reason careful fixation of the free ends of the fascial strips to each other by overlapping and careful suturing would seem important.

In completing the fascial sling beneath the urethra, it has been found that it should be made snug enough to give additional support to the proximal end of the urethra and to be certain of immediate pull forward whenever the recti muscles contract with any strain such as lifting, coughing or sneezing.

DR. JOE V. MEIGS (by invitation).—When looking at the urethra of a patient with incontinence, the orifice points to the ceiling and there is a falling down of the urethra from behind the symphysis. We now begin most of our reconstructive surgery by means of a total abdominal hysterectomy after which we turn the patient around and repair the perineum. For this reason it is necessary to suspend the urethra in a little different way.

In four cases I have done a total hysterectomy and after closing the peritoneum I entered the space of Retzius, pulled the bladder up and exposed the urethra. This is very simple to do and it is very easy to visualize the urethra. It is, however, difficult to get the urethra free from the vaginal wall from above.

In the four cases I was able to go beneath the urethra and in these I took a long strip of the abdominal rectus fascia, threaded it under the urethra, brought it up and attached it to the rectus sheath on the other side. In two of the cases the results were not good at the end of three months, but at the end of nine months, there is a good result in both instances.

The third patient I operated upon by the same method is so continent that I had to dilate the urethra. This patient could void only by placing two fingers in the vagina, one on each side of the urethra, and pulling upward. This patient has had three urethral dilatations and is perfectly comfortable. The fourth patient is temporarily lost to our clinic.

It seems to me that the success Dr. Studdiford and Dr. Aldridge have had is due to the fact that they have repaired the urethra from below, as well as having used a fascial band. In my cases nothing at all was done to the urethra, and in three patients, it worked well. I think the great contribution is the combination of the two operations—a plastic and a fascial sling. I was of the opinion that all that would be necessary would be to suspend the urethra, but I do not think that is sufficient.

DR. FREDERICK C. HOLDEN.—At the time Dr. Aldridge presented his paper, we had on the gynecologic service of the Jersey City Medical Centre, a patient who had been operated on twice in the preceding year—once by a urologist and once by a gynecologist—for urinary incontinence, and she was unimproved after each operation. There was no bulging of her anterior wall, but she had complete urinary incontinence.

It was my good fortune to hear Dr. Aldridge present his paper just during the time that we had her under observation. We operated upon her according to the technique described by Dr. Aldridge, and obtained a perfect result. We saw her in the return clinic several times, the last examination being seven months post-operative, and she reported complete control of her urine under all circumstances.

DR. JOSHUA WILLIAM DAVIES.—It is my belief that the use of fascia *alone* as a transplant around the urethra will not give satisfactory results as an operation for incontinence. Dr. Studdiford has very accurately reconstructed the capsule of the urethra as is shown by his pictures, and if he would utilize the bulbocavernosus muscle as he reconstructs the central body of the perineum, I feel certain that he would secure satisfactory results in 95 per cent of his cases without using the fascial strips.

DR. INGLIS F. FROST.—In some cases where recurrences have occurred there has been, at times, an insufficient preliminary study of the urethra in its relation to the bladder. Dr. Kennedy has clearly shown in his x-ray graphs that the length of the urethra in the incontinent woman, is in disproportion to the neck of the bladder. To obtain a cure in these cases, two factors are important; first, the restoration of the urethra to its normal length and second, mobilization of the bladder in its new position until healing had occurred.

We have used Dr. Kennedy's instrument in numerous cases. It is made of vitallium metal and is composed of two sections, one of which carries gauze in the vagina and retains it. The other acts as a retention catheter. The vitallium metal does not become soiled and no urinary deposits occur. The iodoform packing may remain *in situ* for at least eight days, and thus it acts as a splint to the anterior wall. Constant drainage of the bladder with the vitallium catheter keeps the bladder empty and gives it a chance to heal at the point where you want it to heal.

DR. JAMES R. MILLER.—I would like to say a word in support of the method used by Dr. Hepburn. I have done three cases of complete eversion prolapse of the urethra by this method. The operation is simple and can be done in fifteen or twenty minutes. It has given perfect results in the three cases in which I have done it. The first case was in a woman of 70 with a total prolapse and a large mushroom slough of the urethra. This was pulled back as described by Dr. Hepburn and sutured to the posterior surface of the symphysis and the roof of the bladder above the trigone was sutured to the lower undersurface of the fascia above the symphysis. Later, a LeFort operation was done for the prolapse. That patient has now gone five years and her condition is good.

It is very simple to suture the urethra to the symphysis. A very important step in this operation is to place a drain on each side, to form scar tissue, a point which Dr. Hepburn emphasizes. I hope some day to see this operation for prolapse of the urethra displace the old Whitehead type of procedure.

CAPILLARY COUNTS, CAPILLARY DISAPPEARANCE PRESSURE AND CUTANEOUS LYMPHATIC FLOW IN NORMAL PREGNANCY*

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PREGNANT women frequently experience difficulty in water metabolism. Sometimes they develop hypertension which may or may not subside after delivery. Such a clinical situation offers obvious opportunities for the study of hypertension. Most persons who develop hypertension are first available for study after the hypertension is well established. The pregnant woman is more or less constantly under medical observation and therefore may offer a unique opportunity to study a patient with developing hypertension.

In the present study certain methods which have been applied to the study of patients with hypertension are employed in the study of women in normal pregnancy. These methods include:

1. Capillary counts before and after histamine, by the method first reported by Roberts and Griffith¹ and later by Griffith, Roberts and Corbit.²
2. Capillary disappearance pressure (formerly called minute vessel pressure), as described by Griffith, Roberts and Corbit.³
3. Cutaneous lymphatic flow, as first described by McMaster⁴ and later used by Griffith, Roberts, Rutherford and Corbit.⁵

The present report deals only with women in normal pregnancy without hypertension. It will take somewhat longer to collect data on a corresponding series with hypertension, and the subjects thus far studied are too few to permit their inclusion here.

I. Capillary Counts, Before and After Histamine

The extensor surface of the forearm is used. A circular die is inked and pressed on the skin so that its inked impress encloses an area of normal skin of approximately 2 sq. mm. A drop of cedar oil is placed on this area and the open capillaries counted, using a microscope with Ultrapak attachment as previously described.¹⁻² After a count has been made, a drop of 1:1,000 histamine is placed near the area under observation and a needle pricked through the drop. The flare which

*Read at a meeting of the Obstetrical Society of Philadelphia, March 4, 1943.

†Atwater Kent Fellow in Medicine.

subsequently develops includes the area under observation and the capillary count in it is repeated. The count after histamine is considered to represent 100 per cent of the cutaneous capillaries of that area, and the per cent open before histamine is thus calculated. For example, if, in a given area, 13 capillaries are open before and 26 after histamine, then 50 per cent of the capillaries in that area were open before histamine. A division has been made as follows:

1. Persons with 90 to 100 per cent of their capillaries open before histamine. This group is definitely abnormal and is said to have diminished capillary mobility. It may mean that a degenerative process has involved the capillaries or simply that there is some cause for initial dilatation, as polyeythema, hyperthyroidism, etc.

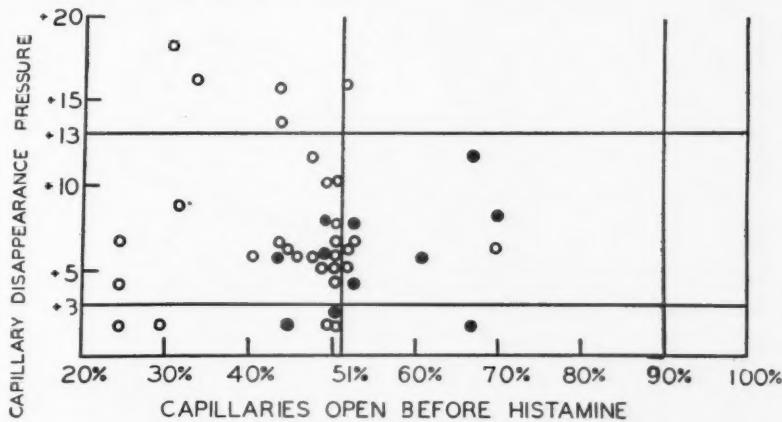


Fig. 1.—Showing relation between increase in capillary disappearance pressure after histamine and number of total capillaries open before histamine. Vertical lines divide the zones of high and moderate capillary mobility (at 51%) and moderate and diminished capillary mobility (at 90%). Horizontal lines at +3 and +13 mm. of mercury indicate the usual limits of rise in capillary disappearance pressure after histamine in normal nonhypertensive subjects. Solid circles indicate subjects with increased cutaneous lymphatic flow, while open circles indicate subjects in whom the cutaneous lymphatic flow was normal.

2. Persons with 51 to 89 per cent of their capillaries open before histamine. This group includes both normal and abnormal subjects, who are said to have moderate capillary mobility.

3. Persons with 50 per cent or less of their capillaries open before histamine. This group is definitely normal, and is said to have high capillary mobility.

The results are shown in Fig. 1. For the moment only the relation of the dots to the abscissa need be considered. It is seen that 30 subjects fell within the group of high capillary mobility, and only 11 in the borderline group with moderate capillary mobility. None showed diminished capillary mobility.

II. Capillary Disappearance Pressure, Before and After Histamine

The method has been previously reported.³ Without repeating details of the apparatus and method, it may be said here that the pressure

recorded is that which when present in a transparent chamber in contact with the skin is just sufficient to cause the disappearance of microscopically observed cutaneous capillaries. The cutaneous area used is the extensor surface of the forearm. While by this method pressure readings can be repeated with variations of not more than 2 mm. of mercury by the same or by different observers, there is considerable doubt as to just what pressure is being measured. On purely theoretical grounds, it seems obvious that it cannot be true capillary pressure. Under conditions of flow, the pressure required to stop flow (or empty a tube which is part of a system of branching tubes) will be the pressure at the nearest bifurcation of the system that has an unblocked branch.

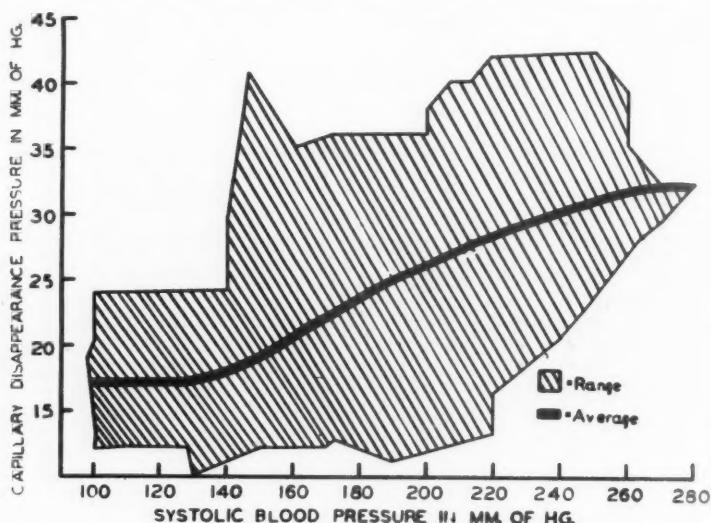


Fig. 2.—Showing the range and average capillary disappearance pressure in subjects with varying systolic blood pressure.

This, most likely, is the precapillary arteriole. It has been shown³ that this pressure will rise to correspond to an increased venous pressure, produced by inflating a blood pressure cuff about the upper arm, and also that it will rise after local procedures, as the injection of histamine. In these respects it behaves like true capillary pressure. The term originally applied³ was "minute vessel pressure" and it was stated that "skin elasticity and resistance may interpose a tangible, but fairly constant factor." More recently, however, evidence has been collected suggesting that extravascular factors may affect pressure readings more than was originally thought, and on this account the term "capillary disappearance pressure," a term that is purely descriptive, has been adopted to replace the term "minute vessel pressure." The reasons for this will be reported, in detail, elsewhere.

Fig. 2 shows the range and average of capillary disappearance in persons with normal and with elevated blood pressure. This chart is

based upon observations on 230 subjects, 71 with normal blood pressure and the remainder with high blood pressure. It will be seen that, for persons with systolic blood pressure below 140 mm. of mercury, the range of capillary disappearance pressure is 10 to 24 mm. of mercury, the average is 17, and the standard deviation is 3.7.

If the measurement of capillary disappearance pressure be repeated in the flare area of a histamine wheal, using the technique described in "capillary counts" it will usually be found that the pressure is higher by 3 to 13 mm. of mercury. Occasionally apparently normal subjects will fail to show any change after histamine, but when this is seen associated with diminished capillary mobility, it is thought to suggest sclerosis of the precapillary arteriole. Occasionally the rise will be more than 13 mm. of mercury, but in the previous report³ this was only seen in subjects with hypertension and was thought to indicate a considerable degree of spasm of the precapillary arteriole.

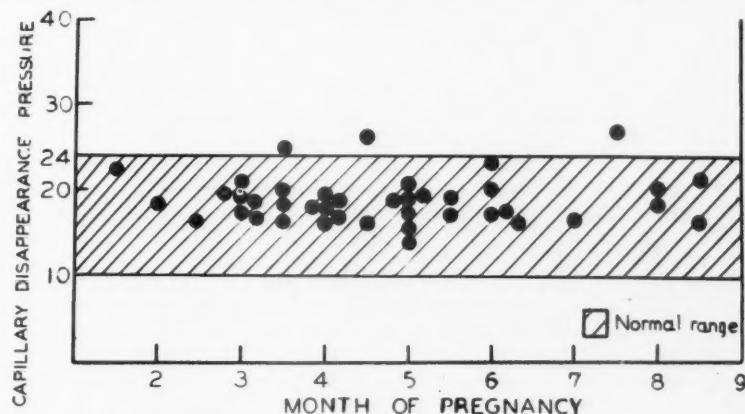


Fig. 3.—Showing the range of capillary disappearance pressure in women at various months of pregnancy. The "normal range" is taken from the nonhypertensive subjects shown in Fig. 2.

Capillary disappearance pressure was measured in a series of pregnant women, and the results are shown in Fig. 3. The systolic blood pressure in every case was below 140 mm. of mercury. Only 3 subjects had a trifling elevation of capillary disappearance pressure, never exceeding 28 mm. of mercury. The average capillary disappearance pressure was 18.5, as compared to 17 for the nonpregnant group. As the deviation from the mean is essentially the same in the two groups, the slight elevation seen in an occasional pregnant subject could have been anticipated.

The increase in pressure after histamine is shown in Fig. 1. While most of the women showed a rise of pressure within the normal limits, it is seen that 7 showed a rise of less than 3 mm. of mercury and 5 a rise of more than 13 mm. of mercury. The latter finding was the more unexpected of the two, suggesting as it did some degree of arteriolar spasm.

III. Cutaneous Lymphatic Flow

The method has been described elsewhere.⁴⁻⁵ Approximately 0.03 c.c. of patent blue, prepared according to the directions of McMaster,⁴ is injected intracutaneously in the flexor surface of the forearm, and its spread noted over a period of 20 minutes. Results are expressed as normal and increased.

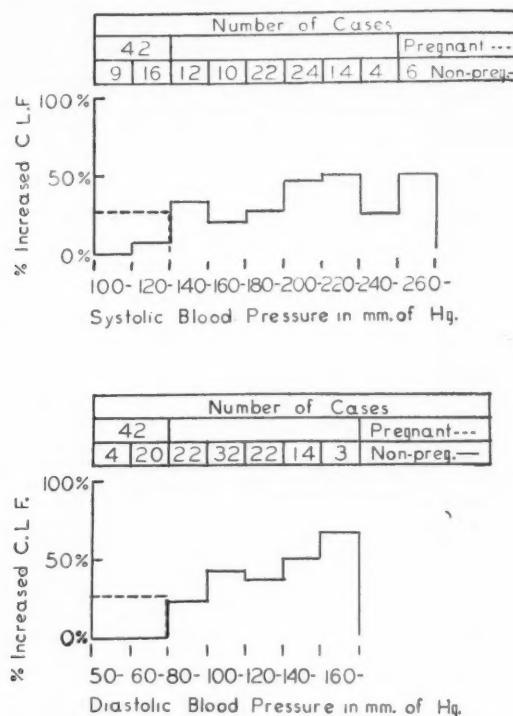


Fig. 4.—Showing the frequency of increased cutaneous lymphatic flow at various levels of systolic and diastolic blood pressure in pregnant and nonpregnant subjects.

The relationship between cutaneous lymphatic flow and systolic and diastolic blood pressure in pregnant and nonpregnant subjects is shown in Fig. 4. It is apparent that in nonpregnant subjects with systolic pressure below 140, increased lymphatic flow occurred in only 4 per cent of the subjects, while in the corresponding pregnant group it was increased in 26 per cent. No nonpregnant subjects with diastolic pressure below 80 showed increased cutaneous lymphatic flow, as compared with 26 per cent of the pregnant subjects.

The relationship between cutaneous lymphatic flow and capillary disappearance pressure in pregnant and nonpregnant subjects is shown in Fig. 5. Here, there is a suggestion that increased cutaneous lymphatic flow, both in pregnant and nonpregnant subjects, is apt to be associated with the higher measurements of capillary disappearance pressure. Considering only those persons with capillary disappearance pressure of 30

mm. of mercury or lower, cutaneous lymphatic flow is increased in 26 per cent of the pregnant subjects and in 19 per cent of the nonpregnant subjects; a difference not significant.

The occurrence of increased cutaneous lymphatic flow, normal blood pressure and normal capillary disappearance pressure, has been observed in a small group of cases included in a report by Pendergrass, Hodes

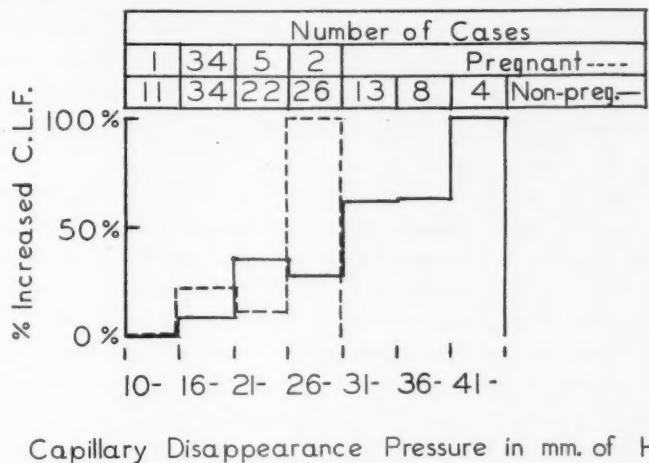


Fig. 5.—Showing the frequency of increased cutaneous lymphatic flow at various levels of capillary disappearance pressure in pregnant and nonpregnant subjects.

and Griffith.⁶ These persons all had edema without evidence of heart or kidney failure or hypoproteinemia. This edema tended to be cyclical and, in women, was frequently associated with the menses. The sera of these persons was able to inhibit the normal water diuresis of rats, and they usually improved or recovered after pituitary irradiation. No such subjects were included in the "nonpregnant" series here reported, which is made up of normal subjects or persons normal except for the presence of a hypertension with its associated phenomena.

Discussion

Increased cutaneous lymphatic flow can, in all probability, be accepted as evidence of increased loss of fluid from the capillaries. This has been discussed previously.⁵ Such increased loss of fluid might result from: (1) Increased capillary pressure. (2) Diminished colloid osmotic pressure. (3) Increased capillary permeability.

The evidence presented by others, especially Dieckmann,⁷ seems to rule out a hypoproteinemia as an etiologic factor. While such measurements were not made in our entire series they were made in 10 cases, and in these there was no evidence that a lowered plasma protein was a factor in the increased cutaneous flow.

Another alternative is that an elevated capillary pressure may be the cause of an increased flow of fluid from the capillaries. This suggestion

requires repetition and elaboration of certain hypotheses previously presented by Griffith, Rutherford, Roberts and Lindauer.⁸

It is probable that rise of intracapillary pressure tends to be limited by a dynamic equilibrium in which outflow from the capillary occurs not only into the vein but also through the capillary wall. The latter phenomenon is, however, limited in rate by the tendency of the colloid osmotic pressure in the capillary to rise as the residual protein becomes concentrated. When fluid is rapidly being lost from the capillaries, as in the first stage of shock, an early physiologic response is an arteriolar constriction which actually lowers capillary pressure and tends to prevent further loss of fluid. This, in general, has been pointed out by Moon.⁹

The gradient of pressure as one passes from large artery to capillary varies with the freedom of flow at each point in the progression. If capillary disappearance pressure is actually, as we think, a measure of pressure in the precapillary arteriole, it may at times be high as the result of arteriolar hypertension, either with or without rapid fall of pressure between the point of measurement and the capillary, depending upon the state of arteriolar tone between the point of measurement and the capillary, and hence with or without a tendency to increased cutaneous lymphatic flow; and impeded flow beyond the capillary may cause rise of capillary pressure with increased lymphatic flow without elevation of pressure so far back as the point at which capillary disappearance pressure is measured. A tendency to correlation between capillary disappearance pressure and cutaneous lymphatic flow would, therefore, be expected, but not perfect correlation.

In Fig. 2 it was shown that in persons with normal blood pressure average capillary disappearance pressure is 17 mm. of mercury. In Fig. 5 it is seen that cutaneous lymphatic flow is not increased, either in pregnant or nonpregnant subjects, until the capillary disappearance pressure exceeds 16 mm. of mercury. By comparison with Fig. 4, it is seen that increased cutaneous lymphatic flow practically does not occur at systolic pressure below 140 and diastolic pressure below 80. Therefore, one may say that in hypertensive subjects as well as in pregnant women increased cutaneous lymphatic flow may occur while capillary disappearance pressure is within the upper half of the normal range, but that the likelihood of its occurrence increases with the rise of the capillary disappearance pressure. Thus it seems most likely that the increased loss of fluid from the capillaries in certain pregnant women is due to a slight increase in capillary pressure.

This evidence has no bearing upon the possibility of a primary increase in capillary permeability.

Summary

Capillary counts before and after histamine, capillary disappearance pressure before and after histamine, and cutaneous lymphatic flow were

measured in a series of women in normal pregnancy, and the results compared with those obtained in normal and hypertensive subjects. All capillary studies tended to be normal, except that occasionally in a pregnant woman the rise in capillary disappearance pressure after histamine was somewhat excessive. Cutaneous lymphatic flow was found to be increased in pregnant subjects when compared with others with corresponding blood pressure, and this showed a rough correlation with the level of capillary disappearance pressure. Theoretical considerations are discussed and the conclusions reached that the increased cutaneous lymphatic flow is most probably due to a slight rise in capillary pressure.

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ENDOMETRIOSIS INTERSTITIALE, WITH A REPORT OF THREE CASES*

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IN 1937 J. R. Goodall^{1, 2} focused attention on a group of uterine tumors which he considered a type of endometriosis in which the stromal cells predominated to the exclusion of the glandular elements. He designated this condition as *endometriosis interstitiale*. The tumors occurred either in the form of a diffuse infiltrative process, or as a circumscribed mass resembling a soft fibroid. Microscopically, they were characterized by an abundant proliferation of a spindle-cell stroma containing numerous thick-walled blood vessels of muscular type. The first case to be reported in the literature was by Casler³ and appeared in 1920. Three instances were also reported by Frank⁴ in 1932.

The present paper deals with three similar cases which were observed in the Hartford Hospital during the past two years. The frequency of occurrence of this lesion obviously cannot be indicated from the available literature. However, the following figures give some idea of the activity of the Hartford Hospital in this field. During the years 1940, 1941, and 1942, seven hundred fibroid uteri were examined in the laboratory, while in the same interval a gross diagnosis of endometriosis was made at operation in 179 cases with microscopic confirmation in 90. Since other reports have indicated that these tumors have been mistakenly classified as myosarcomas, a review of the sarcomas of uteri at the Hartford Hospital was made but failed to reveal any additional instances of stromal-cell endometriosis.

The present report seems warranted because of the apparent rarity of the condition and to emphasize the anatomic features which establish the correct diagnosis.

CASE 1.—(H. H. 426-676.†) J. M., a 22-year-old single, American girl, was admitted to the ward service of the Hartford Hospital on February 2, 1942 with a diagnosis of incomplete abortion. She had missed her period in November but menstruated again in December and January. The last period occurred a week later than expected and was accompanied by unusual cramps in the lower abdomen. Following this period, she continued to spot until her admission two weeks later. She had experienced no fever and denied instrumentation. Her past history was not contributory. On February 7, a curettage was done. The uterus was enlarged, globular, smooth, freely movable, and lying in an anterior position. No masses were found in the adnexal or parametrial regions. The cervix was firm. The uterine sound entered the cavity a

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†Reported by Dr. Louis Middlebrook, Connecticut S. M. J. 7: 544, 1943.

distance of 7.5 cm. After dilatation the cavity was explored with an ovum forceps. No tissue was obtained at first, but finally, a portion of a firm smooth mass (specimen I) was removed with a sponge forceps. The patient was discharged from the hospital a few days later. The tissue removed was examined and a diagnosis of endometriosis interstitiale was made.

The patient was readmitted February 16, and the entire uterus and both tubes removed (specimen II). (Fig. 1.) The ovaries appeared normal and contained numerous follicular cysts. There were no adhesions or enlarged glands. She was discharged on the twenty-first hospital day.



Fig. 1. Case 1.—Uterus opened showing polypoid tumor mass in fundus.

Pathological Report. Specimen I.—*Gross:* The specimen was a polypoid mass of firm gray tissue which measured 2.5 by 1 by 1 cm. The surface had a hemorrhagic appearance.

Microscopic: Sections showed a tumor composed of delicate spindle-shaped cells arranged in interlacing strands. The cells had deep blue vesicular nuclei and showed occasional mitoses. In some portions, the cells were closely packed, but in other parts were separated in a coarse reticulated pattern. There were many thin-walled dilated vascular channels in these regions which suggested lymphatic structures. A more striking feature was the presence of numerous thick-walled blood vessels of arterial type which were found in the more cellular portions of the tumor (Fig. 2). The arrangement of these vessels in groups resembled the spiral arteries of the endometrium. No glandular elements were present. Silver stains for reticulum showed a network of fibers which formed a basket-weave pattern about the individual cells. This arrangement resembled that of the stroma of the normal endometrium. A diagnosis of endometriosis interstitiale was made.

Specimen II.—Gross: The specimen consisted of uterus with cervix and tubes attached. The uterus which was slightly asymmetric and enlarged, measured 10 by 5.5 by 3.5 cm. The cervix was small, the os was round, and the endocervix was lined by a smooth pale mucous

membrane. When the uterus was opened, a pedunculated soft red-brown mass was found projecting into the uterine cavity from the fundus (Fig. 1). This papillary mass measured 4 cm. in length. Its cut surface was a soft pale pink. The tumor extended into the myometrium at the point of attachment although the boundary between the tumor and myometrium was sharp.

At one point an isolated tongue of tumor tissue projected above the cut surface of the myometrium beyond the line of attachment of the main mass of tumor. This appeared to project from a dilated vascular channel into which it had grown. The tip of the polypoid mass was hemorrhagic and ulcerated. The endometrium in other portions of the uterine cavity was pale and atrophic. The Fallopian tubes were normal.

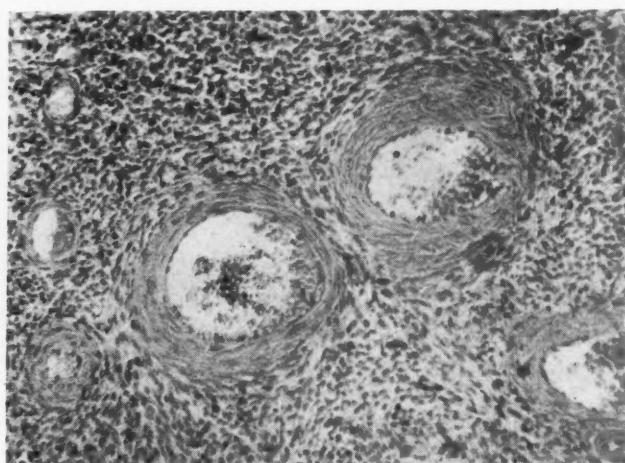


Fig. 2. Case 1.—Cellular spindle-cell stroma with thick-walled blood vessels. H. & E. ($\times 180$).

Microscopic: The tumor presented histologic features which were identical with those of the previous biopsy specimen. There was a sharp line of demarcation between myometrium and the tumor. At one point a tongue-like growth of tumor projected into a dilated vascular channel. It was covered by flattened endothelium which was invaginated by the tumor growth into the vessel's lumen.

Comment: The gross and histologic appearance of this tumor was that of a neoplasm of low malignancy arising from endometrial stroma. The anatomic features were identical with those described by Goodall and others as endometriosis interstitiale. The patient although retaining both ovaries was well and free of signs or symptoms referable to the pelvis when last seen in September, 1943. She stated that her breasts reacted each month with swelling and tenderness as they had formerly at each period.

CASE 2.—(H. H. 453-891.) E. M., a 43-year-old white, American housewife, was first admitted to the Hartford Hospital on March 6, 1943. She had been married many years but never pregnant. She had begun to menstruate irregularly fifteen months before admission, though her periods up to that time had been regular with moderate dysmenorrhea. She flowed constantly from January to June, 1942 when she had three sudden hemorrhages of bright red blood and clots. In June, 1942 she was operated on in another hospital and a mass which was thought to be

a cervical fibroid (specimen I) was removed. A pathologic diagnosis of submucoid leiomyoma was made.

After this operation her periods became regular but more prolonged than usual until two months before admission when she again began to bleed constantly. She was referred for hysterectomy by the family physician. Examination upon admission revealed the presence of a black necrotic mass 6 cm. in diameter, lying in the vagina and apparently the cause of a foul, dark, bloody discharge. This mass was attached by a long, fairly firm pedicle to the upper part of the uterine cavity. Hysterectomy was considered unwise in the face of the apparent uterine infection, so under anesthesia the mass was removed with

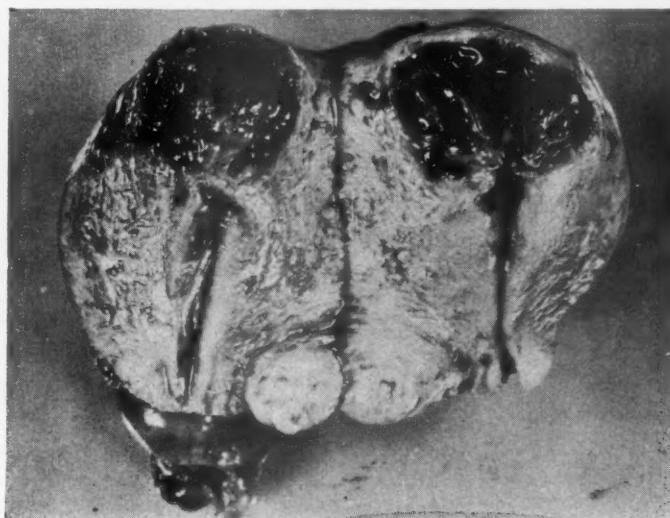


Fig. 3. Case 2.—Structure of tumor removed at first operation (specimen I).
H. & E. ($\times 180$).

the aid of long curved scissors. The mass resembled necrotic products of conception (specimen II). The uterus was packed with gauze containing sulfanilamide crystals, after removal of which, the patient was permitted to go home. Histologic examination of the tissue showed typical stromal-cell endometriosis. She was readmitted on April 6, and the fundus of uterus, tubes, and ovaries were removed, (specimen III). A total hysterectomy had been contemplated but because the patient weighed 210 pounds, had hypertensive heart disease with blood pressure of 240/130 and a cervix which was deeply and firmly held in the pelvis, the less radical procedure was carried out.

Pathological Report. Specimen I.—Gross: The specimen was an irregularly spherical mass 5 cm. in diameter having a hemorrhagic ulcerated surface. The cut surface was composed of soft yellow-pink tissue with numerous cystic zones containing gelatinous material.

Microscopic: The tumor was made up of delicate spindle-shaped cells arranged in an interlacing pattern. Occasional cells showed mitosis. Some thick-walled muscular vessels were present (Fig. 3). Surface of tumor was ulcerated and showed acute inflammatory infiltration.

Comment: This was considered to be an ulcerating submucous fibromyoma of increased cellularity and mitotic activity.

Specimen II.—Gross: The specimen consisted of a mass of blood clot containing several fragments of gray tissue.

Microscopic: Sections revealed a cellular tissue composed of delicate spindle-shaped cells with clusters of thick-walled muscular vessels of arterial type dispersed throughout. The cells resembled those of the endometrial stroma although no glandular elements could be found. They showed frequent mitoses. The surface of the mass was covered by a flattened layer of columnar epithelium. This gave the tissue a polypoid appearance.

Comment: A diagnosis of endometriosis interstitiale was made.

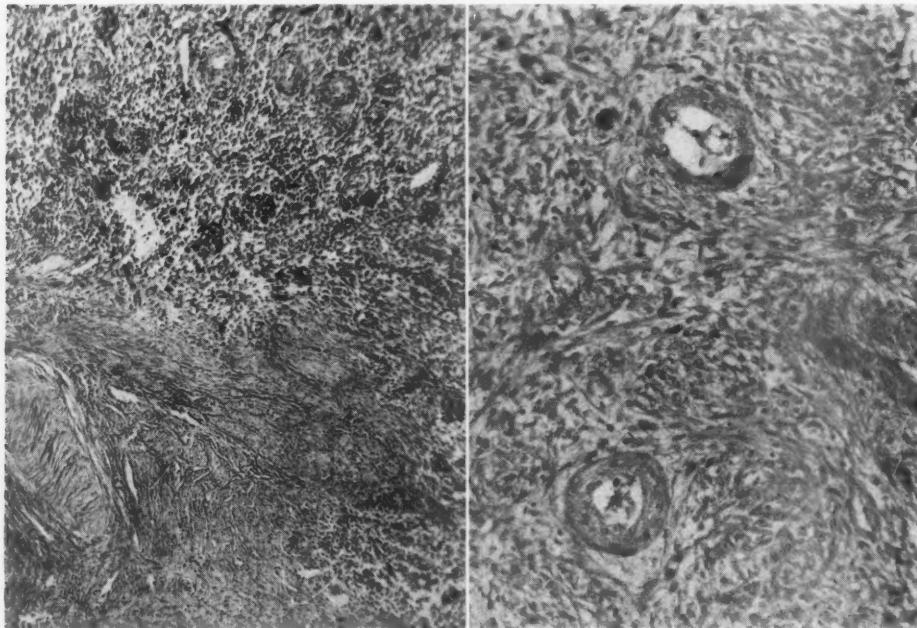


Fig. 4.

Fig. 5.

Fig. 4. Case 2.—Uterus sectioned showing multilocular cystic tumor of myometrium.

Fig. 5. Case 2.—Showing tumor above and myometrium below with indefinite boundary. Cellular stroma with thick-walled vessels are prominent. H. & E. ($\times 80$).

Specimen III.—Gross: The specimen was a supracervical uterus with one tube and ovary. The uterus measured 10 cm. in greatest diameter and was distorted by several small myomatous nodules. On cross section of uterus a sharply circumscribed multilocular cystic tumor 5 cm. in diameter was found in the fundic portion of the myometrium (Fig. 4). This mass had a variegated red and yellow appearance. The cystic spaces contained clear yellow fluid and had delicate walls. The tumor extended to the endometrial lining but there were no polypoid projections into the small uterine cavity. The endometrial lining had a granular red appearance. Several myomatous nodules from 1 to 3 cm. in diameter were also present within the myometrium. The tubes and ovaries had a normal appearance. The ovaries contained simple and follicular cysts.

Microscopic: Histologic sections of the tumor showed masses of small spindle cells resembling endometrial stroma scattered throughout which were clusters of thick-walled blood vessels of arterial type (Fig. 5). The

tumor cells showed rare mitoses. The cystic spaces had a flattened endothelial lining and suggested dilated vascular channels. The tumor infiltrated the adjacent myometrium to some extent, but this was not marked. Silver stains revealed a basket-weave pattern as seen in the first case.

Comment: Review of the three specimens from this case showed that the initial specimen had features similar to the latter two. A silver stain to demonstrate the basket-weave pattern of the reticular network would have aided in establishing the diagnosis at the time of the first biopsy.

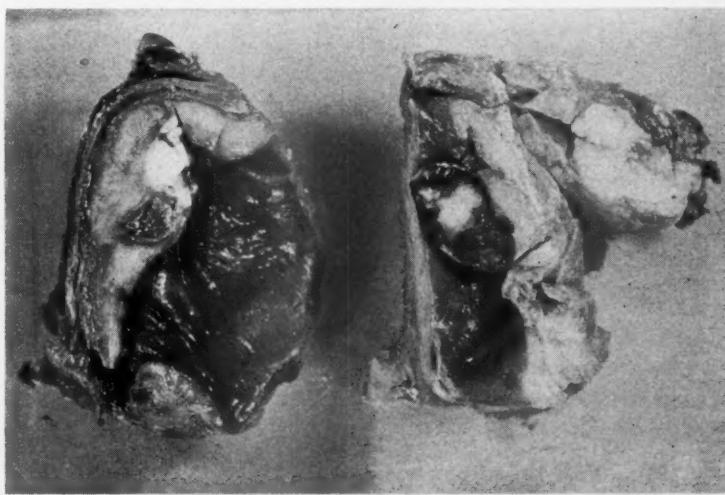


Fig. 6. Case 3.—Section of uterus through large cystic cavity in myometrium.

CASE 3.—(H. H. 455-563.) M. A., a 57-year-old single, white American schoolteacher, was admitted to Hartford Hospital March 25, 1943. Her menopause had occurred at the age of 50 without incident or history of previous menstrual difficulty. She had noted a gradual enlargement of the abdomen during the past six months but thought nothing of this until she began to have abdominal pain and a rapid enlargement of the mass in the lower abdomen during the past two months. She had lost 15 pounds and had been treated for pleurisy two months previously. Examination showed a symmetric, easily movable mass occupying the upper part of the true pelvis, rising to the umbilicus. It felt solid. The introitus was virginal. Remainder of the physical examination revealed nothing of note.

Stereoscopic x-rays of the thorax showed only slight pleural thickening at both bases. Exploratory laparotomy was done with the tentative diagnosis of fibroid of the uterus and possible carcinoma of the ovaries. At operation the upper abdomen was found to be the seat of a large neoplastic mass which was apparently primary in the gall-bladder, with metastases in the omentum, preaortic glands, liver, and peritoneum. The complete excision of the uterus, tubes and ovaries was easily carried out.

The patient left the hospital after an uneventful primary recovery, but died two months later at her home from extensive carcinomatosis.

Pathological Report.—Specimen I. Gross: The specimen consisted of uterus with cervix, tubes and ovaries attached. The uterus was irregularly spherical in shape and measured 15 cm. in diameter. On

its serosal surface, there were several plaque-like thickenings each 1 em. in diameter. These were implants of metastatic squamous-cell carcinoma which were similar to those found elsewhere in the peritoneum at the time of operation. When the uterus was sectioned a large cystic cavity was entered; this contained approximately 500 c.c. of brown blood-tinged fluid in which many cholesterol crystals floated (Fig. 6).

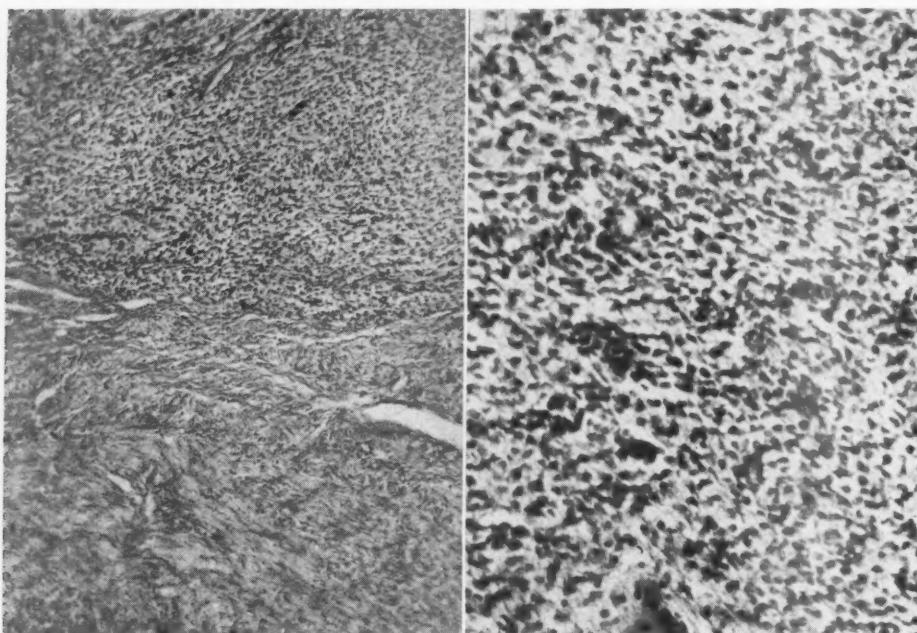


Fig. 7.

Fig. 8.

Fig. 7. Case 3.—Shows spindle-cell lining with junction with myomatous portion of tumor H. & E. ($\times 110$).

Fig. 8. Case 3.—High power of inner cellular zone. H. & E. ($\times 330$).

The lining of the cyst was red-brown and smooth, and in one region a yellow-green irregular mass 7 cm. in diameter projected from the wall into the cavity. The mass was composed of soft, friable tissue and beneath it there was a layer of hemorrhagic tissue 5 cm. in diameter in which no structural detail could be made out. Surrounding the inner layer there was a 1.5 cm. layer which had the gross appearance of a fibroid and which formed a sharp boundary between the tumor and the adjacent myometrium. The endometrial cavity which was elongated and flattened by the cystic mass had no communication with the cyst. The endometrial lining was pale and atrophic. The cervix and tubes were normal. The ovaries were atrophic.

Microscopic: Microscopic sections showed the cyst lining made up of a thick layer of small spindle-shaped cells forming a reticulated pattern. Surrounding this were interlacing bundles of fibromuscular tissue typical of a myoma with a sharp demarcation between this portion and the adjacent myometrium. The inner zone resembled endometrial stroma but no glandular elements could be found (Figs. 7, 8). Silver stains showed a basket-weave pattern similar to normal endometrium. This contrasted strikingly with the myomatous outer portion

which showed the reticulum arranged in parallel strands as in normal myometrium.

Comment: This case appeared to represent a stromal endometriosis which was associated with myoma formation comparable to an adenomyoma but without the glandular elements of the endometrium participating in the process. The metastatic squamous cell carcinoma was unrelated to the uterine condition but resulted in the patient's demise.

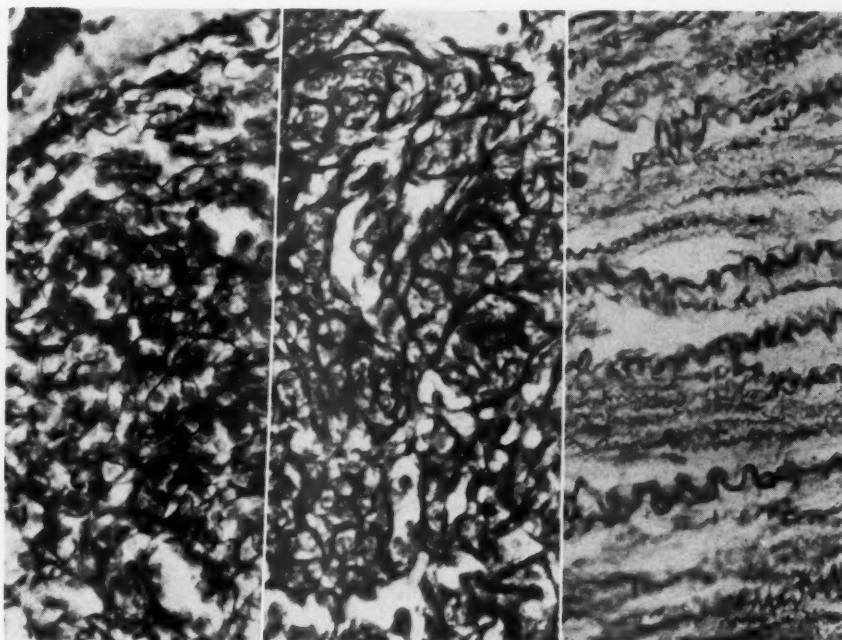


Fig. 9.—Bielschowsky stain for reticulum. ($\times 500$.) *A*, Normal endometrium; *B*, endometriosis interstitiale; *C*, myometrium.

Discussion

The present cases all showed lesions of a circumscribed type. The first was a soft, polypoid mass resembling a submucous fibroid tumor and similar to several others reported in the literature. The other two showed cystic changes which have not been found as a feature of the previously recorded cases. In the second case these spaces had a microscopic appearance which suggested dilated vascular channels. They may have arisen from the abundant vascular component which is a prominent characteristic of these tumors.

Infiltration of the myometrium was not extensive in any of these instances nor was there evidence of anaplasia of the cells or other changes indicative of malignancy. However, as pointed out in Goodall's monograph⁵ and the reports of Robertson et al.,⁶ the disease may pursue a variable course. In some instances the process has assumed a malignant character uncontrolled by operation, ultimately becoming refrac-

tory to irradiation and ending in extensive infiltration of the pelvic tissue which has led to death by obstruction of the ureters. On the other hand, it is essential to differentiate this process from the leiomyosarcomas with their attendant high mortality from extensive metastatic disease. This is especially true in the infiltrative types of stromal endometriosis which have extended into the parametrial tissue where sterilization is of value in retarding the process as in the usual varieties of endometriosis.

The employment of silver stains to show the reticulum pattern as demonstrated by Frank⁴ and emphasized by Feinberg⁷ and Robertson⁶ has proved of especial value. The typical basket-weave pattern of the reticulum of the normal endometrium was well preserved in all three of the present tumors and contrasted distinctly with the arrangement of the reticulum in parallel strands in myomatous tumors (Figs. 9a, b, c). In the second case, the use of the silver stain on the specimen from the first operation would have assisted in establishing the correct diagnosis earlier.

The third case with the combined myoma and endometriosis interstitiale is noteworthy. A diffuse type of process resembling adenomyosis without glandular elements has been reported by Robertson,⁶ Casler,³ and Frank.⁴ In the present instance the possibility that this was originally a circumscribed adenomyoma with glandular elements must be considered, since the patient was seven years past the menopause and atrophy of the glandular components may have occurred.

Summary

Three cases of endometriosis interstitiale of uterus are reported. A feature of two, which has not been previously reported, was the presence of cystic spaces throughout the tumor. The value of silver reticulum stains as an aid in the differentiation from myomatous tumors is emphasized.

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Discussion

DR. ROBERT T. FRANK.—While the cases shown by Dr. Miller correspond to those reported by Casler and Goodall, they differ from those that I reported, as well as those of Robertson, Hunter, Larson and Snyder.

The main features of the three cases which I described are the elevated, yellowish, 'rubbery' areas appearing between coarse fibrous bands on gross cross section of the uterus. Microscopically, these yellowish areas consist of cells which are not

fully characteristic either of endometrial stroma or of endothelial cells. The main microscopic characteristic in my tumors is the distribution within the lymphatic channels, but almost always covered by intact lymphatic endothelium. Clinically, the process is characterized by slow, persistent growth, a long latent period before recurrence. In my first case, the latency persisted for nine years. Therefore, Robertson's deductions, based on cases with a shorter period of observation, are as yet inconclusive.

In summary, I would say that there exists the typical endometriosis in which both glandular and stromal elements are almost equal in number. Then there are cases with a gradual diminution of the glandular elements until stroma far predominates, and finally, but less easily classifiable, cases probably of different etiology, as described by Dr. Robertson and myself.

DR. G. L. MOENCH.—I was very much interested in the cases presented by Dr. Miller. "Stromal Endometriosis" is certainly rare. When we consider that there is no basement membrane between the endometrium and myometrium it would seem as if both glands and stroma, or either one alone, might easily be misplaced into the muscle tissue. Perhaps, however, the fact that the epithelium determines its stroma and that epithelium may come directly from stromal cells, leads in nearly all cases to an intimate association of glands and stroma. Only under peculiar circumstances does stromal tissue continue to exist alone.

Dr. Miller has suggested that perhaps the glands have degenerated. I might add that perhaps they have not yet formed, or we might be dealing with embryologically misplaced tissue similar to a tumor I saw in the broad ligament, which was not connected with the tube or uterus and was made up almost entirely of endometrial stroma. This tumor was about the size of a lemon, was removed at the time of a cesarean section, and showed marked decidual reaction.

When we consider all the vagaries of endometriosis, or adenomyosis, as I prefer to call it, it need not strike us as strange that unusual pictures are encountered at times. One fact, however, stands out in the literature and that is that adenomyosis is practically never malignant. Why then "stromal endometriosis" should show such malignant tendencies is not at all clear. There must be some other factor we have not yet grasped and in this light I am not willing to say that Dr. Miller's cases should be interpreted only as "stromal endometriosis."

DR. JOE V. MEIGS (by invitation).—In going over our uterine tumors at the Massachusetts General Hospital, we found only one case of the type under discussion. This resembled Dr. Frank's cases more than those of Dr. Miller. This patient was about 36 years of age. She had a total hysterectomy done for what was thought to be sarcoma. In going over the slides, we found worm-like areas infiltrating the lymphatics into the broad ligaments and the uterine wall. The patient was alive ten years after operation. When Dr. Goodall wrote his paper I mentioned this patient to him and he sent me an early copy of his report on this subject. Our pathologist agreed that it probably was a sort of endometrial stromal tumor.

DR. TENNANT (closing).—When we first saw the material from the first case we thought we were dealing with a sarcoma probably arising from the myometrium, but we were impressed by the numerous thick-walled blood vessels present in this case and also in our subsequent cases. These findings have been emphasized by Robertson in his paper as a characteristic of stromal-cell endometriosis.

The other point of value to us in differentiating this tumor from the myosarcomatous tumors was the silver reticulum stain which in the three cases showed a distinct basket-weave pattern quite different from the pattern in the myometrial tumors.

THE ELDERLY PRIMIPARA*

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SINCE the publication in 1938¹ of a study of 240 cases of elderly primiparas delivered in the Woman's Clinic of the New York Hospital, many more cases have occurred on this service and more data have been collected on this obstetrical problem. The following study is based on an exhaustive review of 830 elderly primiparas delivered during the eleven-year period from September 1, 1932, to September 1, 1943, and thus includes the 240 cases originally presented. During this period of time there have been 30,880 full-term and premature deliveries in this clinic. Of this number 830 were elderly primiparas, an incidence of 2.68 per cent. An elderly primipara is any patient thirty-five years of age or over delivered for the first time of a viable infant.

In this study 424 patients, or 51.1 per cent of the total cases, were 35 to 36 years of age. There were 104 patients, or 12.5 per cent of the cases, 40 years of age or over. The oldest patient in this group was 46 years of age. There were 27 colored patients in the series, an incidence of 3.3 per cent as compared with 4.9 per cent, the incidence of colored patients in the clinic as a whole. Of the total 830 cases, 342 (41.2 per cent) were private patients. This is in distinct contrast to the higher figure of 91.5 per cent as reported by Erving and Power.²

In this total group of elderly primiparas, 604 (72.8 per cent) were primigravidae. In the remaining 226 primiparas, 149 had spontaneous abortions, 71 had induced abortions, and 6 had ectopic pregnancies. There was a total of 372 pregnancies in this group, one patient having had 8 spontaneous abortions, and another 7 induced abortions.

It has been stated in the literature³ that the longer the period of relative sterility (or infertility), the more difficult the labor, and the more frequent the complication. The factor of sterility or infertility cannot accurately be evaluated since we are unable to determine from the histories studied whether or not contraceptive measures had been employed. Table I shows the results in 207 primigravidae married four years or longer.

Previous to the present admission to the hospital at the time of delivery, 51 patients (6.1 per cent) of the 830 had a major or minor operation for a gynecological condition. Myomectomy had been performed in 13 cases, suspension of the uterus in 9, and a unilateral sal-

*Presented by invitation, at a meeting of the New York Obstetrical Society, January 11, 1944.

TABLE I. OBSTETRIC RESULTS ACCORDING TO YEARS OF MARRIAGE

DURATION OF MARRIAGE	TOTAL CASES	AVERAGE DURATION LABOR	INCIDENCE OF TYPE OF DELIVERY			MORTALITY	
			SPONTANEOUS	VAGINAL OPERATION	CESAREAN SECTION	INFANT	MATERNAL
4 to 6 years	89	20.28 hours	41.6	42.7	15.7	2.24	
7 to 9 years	62	20.49 hours	45.2	40.3	14.5	8.06	1.61
10 to 12 years	31	17.40 hours	48.4	32.3	19.3	9.67	
13 to 15 years	19	16.28 hours	36.8	36.8	26.4	10.52	
16 to 18 years	5	28.33 hours	20.0	40.0	40.0	20.0	
19 years	1	10.00 hours		100.0			

pingectomy and/or oophorectomy in 26, six of the salpingectomies having been performed for ectopic pregnancies.

In this series of elderly primiparas, the same general complications of pregnancy were encountered as in the clinic as a whole. There were 23 patients (2.7 per cent) with rheumatic heart disease. In a five-year study of all clinic patients the incidence of cardiac disease was 3.5 per cent. Myoma uteri occurred in 49 cases (5.9 per cent), as compared with the incidence of 1.9 per cent for the clinic. The size of the myomas varied from small nodules to large intramural and subserous masses. In only 8 cases, however, was "myoma uteri" the indication for cesarean section. The incidence of toxemia was much higher in the elderly primipara group than in the clinic as a whole, the incidence in the former being 13.98 per cent as compared with 7.29 per cent in the latter. The following table shows the incidence of the types of tox-

TABLE II. TYPES OF TOXEMIA IN THE ELDERLY PRIMIPARAS

TYPE OF TOXEMIA	INCIDENCE IN ELDERLY PRIMIPARAS	INCIDENCE IN TOTAL CLINIC
Mild pre-eclampsia	5.18	3.45
Severe pre-eclampsia	2.65	0.75
Eclampsia	0.62	0.20
Renal disease	0.24	0.26
Hypertensive disease	2.28	1.09
Acute yellow atrophy	0.24	0.01
Unclassified	2.77	1.53
Total	13.98	7.29

emias. A study of all other complications encountered in the elderly primiparas did not show any variation in incidence from that found in the total clinic.

The incidence of contracted pelvis in the clinic as a whole, is 9.2 per cent. In the 830 cases of elderly primiparas 108, or 13.0 per cent, had contracted pelvis. It is stated in the literature⁴ that the funnel pelvis is encountered more frequently in the elderly patient. A study of the contracted pelvis in the clinic as a whole showed that the funnel typical pelvis occurred in 28.2 per cent, while in the elderly primipara group it was found in 45.3 per cent of the cases.

Although we have no statistical information available at this time, we feel that x-ray pelvimetry is indicated in all cases of elderly primip-

aras inasmuch as it gives more information about the pelvis than can be obtained through the clinical methods ordinarily employed. We have used a modification of the Caldwell-Moloy technique of x-ray pelvimetry in this clinic during the past few years, and utilized this method in 150 cases of elderly primiparas. The distribution of these cases as to the suggested and ultimate types of delivery was found to be too scattered to yield any statistical conclusions at this time.

It has been the general impression that when the elderly primipara goes beyond the expected date of confinement (E.D.C.), the labor is usually prolonged and a difficult delivery can be expected. The following table shows the time relationship of the day of delivery to the expected date of confinement.

TABLE III. RELATIONSHIP OF EXPECTED DATE TO THE DAY OF DELIVERY

DAY OF DELIVERY	TOTAL CASES	INCIDENCE
15 days or more before E.D.C.	123	14.8
1 to 14 days before E.D.C.	283	34.1
Delivered on E.D.C.	37	4.5
1 to 14 days after E.D.C.	290	34.9
15 days or more after E.D.C.	83	10.0
E.D.C. unknown	14	1.7
Total	830	100.0

It is noted that 10.0 per cent of the patients delivered 15 days or more beyond the expected date, the longest period being 45 days.

The 83 patients that delivered 15 or more days past term have been studied in detail and the results compared with those of the entire group of 830 elderly primiparas as well as with the figures for the clinic as a whole. The results are shown in the following table.

TABLE IV. RESULTS IN PATIENTS DELIVERING 15 DAYS OR MORE BEYOND E.D.C.

	83 CASES	830 CASES	TOTAL CLINIC
Average duration of labor	24.19 hours	20.41 hours	18.00 hours
Incidence of prolonged labor	28.91 %	17.59 %	9.1 %
Incidence of operative delivery	69.87 %	55.54 %	24.3 %
Incidence of cesarean section	15.66 %	13.37 %	2.9 %
Incidence of infantile mortality	24.09 %	7.64 %	3.71 %
Average weight of infant	3,415 Gm.	3,380 Gm.	3,350 Gm.

The definition of prolonged labor in this clinic is a labor lasting 30 hours or more. The longest labor among the 83 cases was 109 hours and 50 minutes, the shortest 2 hours and 20 minutes, as compared to 109 hours and 50 minutes and 1 hour and 45 minutes, respectively, for the total elderly primipara group. The incidences of prolonged labor and infantile mortality were high in this group of patients that delivered 15 or more days past the expected date of delivery. The incidence of infantile mortality in this group of 83 cases was 24.09 per cent; 8.43 per cent occurred in the patients having a labor lasting less than 30 hours, and 15.66 per cent in the prolonged labor group. These factors of increased fetal mortality and prolonged labor would indicate that the

primipara who falls into this classification should be considered for a more radical type of treatment.

In this study of 830 cases, vertex presentation was found to occur in 91.8 per cent of the cases and breech in 7.2 per cent. The incidence of breech presentation in the clinic as a whole is 4.72 per cent. There were 60 cases of primary breech presentation in this study and only 7 were associated with myoma uteri. Of the breech presentations 40 cases (66.6 per cent) were delivered by breech extraction, and 20 cases (33.3 per cent) by cesarean section. The gross infantile mortality rate in the 40 cases of breech extraction was 22.5 per cent as compared to 13.3 per cent in the breech extractions in the total clinic population. In the 20 cases delivered by cesarean section there were no infantile deaths. Another recent paper from this clinic has reviewed in detail 55 cases of primary breech presentations occurring in elderly primiparas.⁵ The incidence of posterior position in 762 vertex presentations was 15.2 per cent as compared with 8.7 per cent in the total clinic. On admission to the hospital at the onset of labor 60.7 per cent of the vertex presentations were engaged and 39.3 per cent nonengaged. In a previous report⁶ the incidence of nonengagement of the head in a control series of patients was 20.9 per cent. The incidence of operative delivery was 59.9 per cent in the group of elderly primiparas when the head was not engaged at the onset of labor, and the incidence of cesarean section was 22.6 per cent.

The incidence of premature rupture of the membranes in this study was 36.1 per cent, which figure is the same as that for the total clinic population. The definition of premature rupture of membranes in this clinic is rupture of the membranes before or coincident with the onset of labor. There were 7 patients who developed an intrapartum infection, and six of these occurred in the prolonged labor group. The membranes had ruptured prematurely in three of these cases. When the labor is prolonged, the incidence of puerperal infection and infantile mortality increases. The following table shows these incidences.

TABLE V. EFFECT OF PROLONGED LABOR

DURATION OF LABOR	INCIDENCE OF INFECTION		INCIDENCE OF INFANT MORTALITY
	INTRAPARTUM	PUERPERAL	
1 to 29 hours	0.2	5.6	4.3
30 hours or more	4.1	19.8	13.0

The type of delivery in the elderly primipara is one of the most important problems that confronts the obstetrician. Table VI shows the types of delivery employed in this clinic, and compares the incidence with those occurring in the clinic as a whole.

From this table it is seen that the incidence of operative delivery is 55.5 per cent as compared to 24.34 per cent for the total clinic. Piper forceps on the aftercoming head were employed in 5 cases of breech

TABLE VI. TYPE OF DELIVERY

TYPE OF DELIVERY	INCIDENCE	
	ELDERLY PRIMIPARA	TOTAL CLINIC
Spontaneous	44.5	75.66
Forceps: low	24.7	12.19
mid	11.4	3.82
high	0.2	0.02
Breech extraction	4.8	4.08
Version and extraction	0.5	0.45
Craniotomy	0.5	0.15
Cesarean section	13.4	2.91
Other types	0.0	0.72

extraction, Dührssen's incisions were performed in 10 cases and manual removal of the normally implanted placenta was done in 11 cases (1.5 per cent as compared to 0.6 per cent for manual removal in the total clinic). There were 3 instances in which forceps delivery was attempted and failed; two of these cases were delivered by version and extraction, and in the other a craniotomy had to be performed. There were 97 patients who received a medical induction either to stimulate or initiate labor. Thirty-five of these received intranasal pituitrin (pitocin). Of the 97 patients 41 delivered spontaneously, 56 had operative deliveries, and there were 15 infantile deaths. The medical induction was successful in 53 cases. A Voorhees bag was used in 6 cases, and a Wales bougie in one case.

There were 111 cesarean sections in this group of 830 elderly primiparas, an incidence of 13.4 per cent. The types of cesarean sections employed are shown in the following table.

TABLE VII. TYPE OF CESAREAN SECTION

TYPE	CASES	INCIDENCE
Classical	37	33.3
Low cervical	64	57.7
Radical	7	6.3
Ricei	1	0.9
Waters	1	0.9
Latzko	1	0.9
Total	111	100.0

Following the cesarean section, myomectomy was performed in five patients in whom the indication for the operation was not myoma uteri. Hystereectomy was performed in seven instances, five because of myoma uteri, one because of an abnormality of the uterus (uterus didelphys), and one because of failure of the uterus to contract following the removal of the placenta with an associated hemorrhage. Table VIII shows the indications for the cesarean sections.

In the 111 patients who had cesarean sections, 68 (61.2 per cent) had no labor before the operation was performed. In this group there was only one infantile death. The infant, which was premature, died on the thirty-second day of life from an infection of the umbilicus. There were three maternal deaths due to generalized peritonitis. In the cesarean

TABLE VIII. INDICATION FOR CESAREAN SECTION

INDICATION	NUMBER OF CASES
Contracted pelvis	18
Cephalopelvic disproportion	20
Elderly primipara	6
Breech presentation	8
Presentation (2 transverse, 1 compound)	3
Ruptured membranes (6 no labor, 2 no progress with labor)	8
No progress after a trial of labor	8
Cervical dystocia	5
Myoma (7 fundal, 1 cervical)	8
Previous myomectomy	1
Ovarian cyst	1
Toxemia (6 pre-eclampsia, 4 hypertensive, 2 unclassified)	12
Eclampsia	1
Acute yellow atrophy	2
Placenta previa	5
Premature separation of the placenta	3
Cardiac disease	1
Pott's disease	1
Total	111

section group of 43 cases in which there had been some labor preceding the operation, there were three infantile deaths, one from multiple congenital anomalies not compatible with life, and two neonatal deaths from pulmonary atelectasis. There were two maternal deaths in this group. These findings are presented in the following table.

TABLE IX. INFECTION AND MORTALITY RATES IN CESAREAN SECTION

	TOTAL CASES	INCIDENCE		
		PUERPERAL INFECTION	MORTALITY	
Without labor	68	29.4	1.5	4.4
With labor	43	39.5	6.9	4.6
Total sections	111	33.3	3.6	4.5

The following table shows the incidences of the type of delivery and of the infantile and maternal mortality for each age group.

TABLE X. RESULTS ACCORDING TO AGE GROUPS

AGE	TOTAL CASES	INCIDENCE				AVERAGE DURATION LABOR (HOURS)	
		TYPE OF DELIVERY	CESAREAN SECTION	MORTALITY			
		SPONT.	OPERATIVE	INFANT	MATERNAL		
35	244	50.0	50.0	8.6	9.0	0.0	20.57
36	180	41.7	58.3	10.5	5.5	0.6	21.22
37	149	44.3	55.7	11.4	7.3	0.7	20.76
38	87	39.0	60.9	16.1	12.6	1.1	21.24
39	66	43.9	56.1	24.2	1.5	1.5	18.80
40	48	45.8	54.2	16.7	8.3	2.1	17.87
41	25	40.0	60.0	20.0	8.0	0.0	20.25
42	21	28.5	71.5	38.1	4.7	4.7	18.84
43	6	33.3	66.7	50.0	0.0	0.0	19.66
44	2	50.0	50.0	0.0	0.0	0.0	11.16
45	1	100.0	0.0	0.0	0.0	0.0	26.20
46	1	100.0	0.0	0.0	100.0	0.0	10.05

Episiotomy was performed in 65.5 per cent of the vaginal deliveries and a third-degree tear of the perineum occurred in 0.5 per cent of the

cases. In the clinic as a whole the incidence of episiotomy is 55.0 per cent and of third-degree lacerations 0.9 per cent. In this clinic the loss of 600 c.c. or more of blood (excluding cesarean section) constitutes a post-partum hemorrhage. The incidence in this series was 6.0 per cent as compared to 2.3 per cent for the clinic as a whole. Most of the hemorrhages were due to uterine atony. Analgesia during labor was given in 60.7 per cent of the cases. The types used either alone or in combination were morphine, scopolamine, sodium pentobarbital, paraldehyde, and rectal ether. There was no instance where a fetal death could be attributed to the type of analgesia employed. Gas, oxygen, and ether was the anesthetic most frequently used; 78.6 per cent of the patients received this combination at delivery. Ethylene, cyclopropane, ether, avertin, gas-oxygen or local were used either alone or in combination in the remaining cases.

In the 830 elderly primiparas, the incidence of puerperal infection was 12.04 per cent and of puerperal morbidity 13.61 per cent as compared to 6.0 per cent and 7.9 per cent, respectively, for the clinic as a whole. By puerperal infection is meant a rise in temperature to 100.4° F. (38° C.) occurring once during each of two twenty-four-hour periods following delivery or remaining elevated longer than twenty-four hours, excluding the first twenty-four hours after delivery, unless the rise in temperature is definitely proved to be due to other causes such as mastitis, pyelitis or intercurrent infection. Morbidity includes all cases of puerperal infection and all those febrile from other causes. The following table shows the distribution of the types of morbidity.

TABLE XI. PUERPERAL MORBIDITY

CAUSE	CASES
Puerperal infection	100
Febrile, mastitis	4
Febrile, pneumonia	3
Febrile, urinary tract	5
Febrile, other	1
Total	113
Incidence, puerperal infection, 12.04 per cent	
Incidence, puerperal morbidity, 13.61 per cent	

The following table shows the complications of pregnancy that occurred either during the ante-partum or post-partum period.

TABLE XII. COMPLICATIONS OF PREGNANCY AND THE PUEPERIUM

COMPLICATION	NUMBER OF CASES	INCIDENCE
Ante-partum bleeding	13	1.6
Premature separation of placenta	3	0.3
Placenta previa	5	0.6
Urinary tract infection	19	2.3
Thrombophlebitis	8	0.9
Toxic psychosis	1	0.1
Postoperative ileus	5	0.6
Peritonitis	5	0.6
Prolapsed cord	2	0.2
Mastitis	4	0.4
Pneumonia	5	0.6

It is seen from this table that the incidence of ante-partum bleeding is 1.6 per cent; in the clinic as a whole it is 1.3 per cent. The incidences of premature separation of the placenta and placenta previa are 0.3 per cent and 0.6 per cent, respectively, as compared to 0.4 per cent and 0.5 per cent in the total clinic population.

There were six maternal deaths in the group of 830 elderly primiparas. The incidence of maternal mortality is, therefore, 0.72 per cent (7.2 per 1,000 pregnancies) as compared to 0.16 per cent (1.6 per 1,000 pregnancies) for the clinic as a whole. In five of these six cases, death occurred following cesarean section. Three of the deaths were due to infection. These occurred in two classical cesarean sections and in one low cervical section, the indications for the operations being acute yellow atrophy, contracted pelvis, and myoma uteri. None of these patients had had any antecedent labor. The ages of these three patients were 36, 38, and 42, respectively. The fourth death was due to hemorrhage following a low cervical section performed after 15½ hours of labor, the indication being cephalopelvic disproportion. The age of this patient was 40 years. The fifth death was due to cerebral embolus which occurred on the fifth postoperative day. This patient, aged 37, had a low cervical section after 21 hours and 56 minutes of labor without progress. The sixth patient, aged 39, died 55 minutes after a full-term mid-forceps delivery which was performed after 27 hours of labor because of fetal distress. Death in this case was due to circulatory collapse which was presumed to have been precipitated by a pituitrin reaction. The three patients in whom death was due to infection following cesarean section had no labor preceding the operation. One patient developed a generalized peritonitis with intestinal obstruction which necessitated an ileostomy. Death occurred on the twelfth postoperative day. The other two patients of this group died on the seventh and tenth postoperative days, respectively; one had, in addition, a femoral and pelvic thrombophlebitis. The deaths from peritonitis all occurred before the advent of sulfonamide therapy. In at least two of the six cases, death might have been obviated. In the case of the death from hemorrhage, the course undoubtedly would have been altered by more expeditious and intensive treatment of the accompanying shock. In the case of the cesarean section performed because of myoma uteri, more radical surgery would appear to have been indicated. Recent studies⁷ have shown that in the presence of large myomas of the uterus, the morbidity and mortality rates following cesarean section are diminished if hysterectomy is performed. The following table shows the incidence of mortality in the entire group and in the cesarean section group.

TABLE XIII. MATERNAL MORTALITY

	INCIDENCE	
	TOTAL GROUP	CESAREAN SECTION
Elderly primiparas	0.72	4.49
Total clinic	0.16	1.52

It has often been thought that the weight of the infant of the elderly primipara is greater than average. We have not found this to be true. The average weight of the full-term infants in this series was 3,380 grams, and the average weight for full-term infants in the clinic as a whole is 3,350 grams. The largest infant among the elderly primiparas weighed 5,200 grams and the smallest 1,190 grams. There were 8.2 per cent of the infants that weighed 4,000 grams or over as compared to 10.5 per cent for the clinic as a whole. The incidence of premature infants was 6.0 per cent as compared with 3.6 per cent for the clinic. This greater incidence of prematurity has been reported by others in the literature.⁸ There were six sets of twins in the entire group. With regard to the sex of the infants, 51.3 per cent were males and 48.7 per cent females, a ratio of 106:100.6.

In this study of 830 cases (836 infants) there were 64 infantile deaths, an incidence of 7.65 per cent as compared to 3.71 per cent for the clinic as a whole. There were 43 autopsies (67.1 per cent) performed, but no definite cause of death could be found in 35 per cent. There were 45 deadborn infants, 3 stillborn, and 16 neonatal deaths. The following table shows the time of death in utero of the 45 deadborn infants.

TABLE XIV. TIME OF INTRAUTERINE DEATH

TIME	CASES	INCIDENCE
Before onset of labor	15	33.3
During first stage	20	44.5
During second stage	10	22.2
Total	45	100.0

It can be seen that in 66.6 per cent of these cases death occurred during labor. Since 22.2 per cent occurred during the second stage, it would follow that interference at an earlier time would have been justifiable. The causes of death in this group were three intracranial injuries, three intrauterine asphyxia of which the cause was not clear, one asphyxia due to loops of cord around the neck, and three unknown. The types of delivery in this group were: three midforceps (one with Dührssen's incisions), three low forceps, one high forceps with Dührssen's incisions, one failed forceps with craniotomy, and two breech extractions.

The following table shows the cause of death and type of delivery in the infantile mortality group.

TABLE XV. INFANTILE MORTALITY

CAUSE OF DEATH	NUMBER OF CASES			
	DEADBORN SPONTA- NEOUS	AND STILLBORN OPERATIVE	NEONATAL SPONTA- NEOUS	DEATH OPERATIVE
Intracranial hemorrhage	0	6	0	3
Congenital anomalies	2	1	2	1
Asphyxia	1	3	0	3
Pneumonia	1	0	0	2
Unknown	15	19	3	2
Total	19	29	5	11

Of the 785 live infants discharged from the hospital, 51 had some complications. There were 16 with congenital abnormalities, such as clubfeet, harelip, and cleft palate or imperforate anus. Eight infants had an infection—impetigo, diarrhea, or thrush. Four others had hemorrhagic disease. There were 23 with traumatic injuries; five of these had cerebral hemorrhage. The other injuries were fractured clavicle or humerus, cephalhematomas, and brachial palsy.

Discussion

It is quite evident from the figures presented in this paper that the results obtained in the care and delivery of the elderly primipara can be improved. From the time the patient first presents herself for obstetrical care until after delivery, she must be carefully studied and closely followed. Detailed information must be obtained concerning the pelvis, and at term the size of the infant estimated as accurately as possible. The expected date of delivery must be ascertained, for it is seen that in patients who go more than two weeks past term, the labor is longer and the infant mortality higher. In patients who do go past the expected date, operative interference should be considered, especially if any complication is present. A normal individual who marries late in life and who is delivered of a full-term or premature infant at 35 years of age or over, may have no complications at the time of delivery. In patients giving a history of a long period of infertility, without the use of contraceptives, operative delivery should be carefully considered. In the older patient myoma uteri and toxemia are the two most frequent complications to be found. The incidences of operative procedures and of infantile and maternal mortality are much higher in this group of elderly primiparas, but as our knowledge of obstetrics progresses, we feel these can be readily improved. Conservative treatment is at all times the best policy to follow, but very often what seems to be a radical procedure, in the case of the elderly primipara becomes a conservative one.

Summary and Conclusions

1. The incidence of elderly primiparas in this clinic was 2.68 per cent.
2. The incidence of toxemia of pregnancy in these patients was 13.98 per cent as compared to 7.29 per cent in the clinic as a whole.
3. Myoma uteri occurred in 5.9 per cent of the elderly primiparas as compared with 1.9 per cent in the total clinic.
4. Although the incidence of contracted pelvis in this series was 13.0 per cent in contrast to 9.2 per cent for the total clinic, the greatest difference appeared in the incidence of funnel pelvis. This type made up 45.3 per cent of the contracted group in the elderly primiparas and 28.2 per cent in the clinic.
5. When the elderly primipara goes two weeks or more past the expected date of delivery, the incidence of prolonged labor is 28.91 per

cent, of operative delivery 69.87 per cent and of infantile mortality 24.09 per cent, as compared with 17.59 per cent, 55.54 per cent and 7.64 per cent, respectively, for the entire group of elderly primiparas.

6. The average duration of labor for this group was 20.41 hours. The average duration of labor for primiparas in the clinic is 18.0 hours.

7. The incidence of operative deliveries was 55.54 per cent and of cesarean section 13.38 per cent, while in the clinic as a whole, these incidences are 24.3 per cent and 2.9 per cent, respectively.

8. The gross infantile mortality was 7.64 per cent as compared to 3.7 per cent for the clinic as a whole.

9. The maternal mortality was 7.2 per 1,000 pregnancies as compared to 1.6 per 1,000 pregnancies for the total clinic.

10. The mere fact that a patient is an elderly primipara is not in itself an indication for cesarean section. If, however, there is an added factor which under any circumstance would be an indication for cesarean section or would increase the fetal mortality rate, this operation is justifiable. For it is recognized that in selecting the type of delivery for this group of patients, the greater importance of the fetus does play a role. This is especially true when the patient gives a long history of relative sterility or of repeated spontaneous abortions.

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Discussion

DR. GEORGE H. RYDER.—The statistics just given were compiled from ward patients. It might be of interest to compare these with statistics compiled entirely from private patients. In my first 1,400 consecutive deliveries of private patients, the incidence of elderly primiparas was about 1 in 24 (4.2 per cent). Comparison with the whole series of 1,400 women shows the following:

The incidence of toxemia of pregnancy was 3 times higher, as was that of eclampsia. The incidence of occiput posterior positions was 50 per cent higher, while that of spontaneous rotation was lower (one-fourth of all in contrast to over one-third).

The incidence of operative deliveries was much higher, over three-fourths in contrast to less than one-third. Cesarean sections constituted one-fourth in contrast to 3.7 per cent; and forceps deliveries over one-half in contrast to one-fourth. The incidence of high forceps was more than 3 times as great, that of medium forceps over twice as great, and that of low forceps more than 50 per cent greater.

The incidence of placenta previa was 3 times higher; that of prolapsed cord 5 times higher; and that of tamponade of the uterus in pelvic deliveries, $2\frac{1}{2}$ times higher. Fibroids were found in about 1 out of every 5 elderly primiparas.

The average length of labor was considerably greater. The incidence of long labors (36 hours or more) was 3 times higher. The total fetal mortality was almost twice as high; that from dystocia 3 times as high, and that from other causes 50 per cent higher.

Among the 1,419 babies of the series, there were 8 hopeless defectives. Two of these, Mongolian idiots, were among the babies of the 59 elderly primiparas, an incidence 6 times higher.

The morbidity (temperatures of 100.6 F. for 48 hours) among the elderly primiparas was more than 3 times higher than among the women of the whole series, that from puerperal causes $3\frac{1}{2}$ times higher, and that from nonpuerperal causes 3 times higher. The maternal mortality was more than 12 times higher, the two deaths occurring among the 59 elderly primiparas being half of all maternal deaths among the whole series of 1,400 women. Among these 1,400 women, only one young woman died, from grippe pneumonia in the epidemic of 1918. The other three deaths were in women at or near the age of forty, 1 from pulmonary embolus, 1 from pneumonia following toxemia of pregnancy, and 1 from a ruptured appendix with operation refused.

It seems clear that elderly primiparas, not only have harder times in labor, but that they are more susceptible to complications in pregnancy and the puerperium.

DR. EDWARD G. WATERS.—This presentation is of immediate clinical interest for we see a large number of elderly primiparas in contrast to years ago. The elderly primiparous patient is interested in her chances as compared to those of her sister fifteen years younger. From a purely obstetric standpoint, her outlook is little if any worse than that of a girl of twenty who happens to be pregnant, if one accepts the fact that she is fifteen years older and subject to all the hazards that the process of getting older entails.

I have been interested in this problem and in the last year Dr. Wager and I have been checking the elderly primiparas at the Christ Hospital. We have taken the same age standard of 35 years or more for classifying these women as elderly and we have some rather interesting data. We do not see nearly as many in our clinic, proportionately, of these elderly or old primipara as recorded here tonight. In our hospital there were only 312 in 25,860 deliveries.

It is hard to tell when a woman is old from the standpoint of having babies. We wished to have data by which we could compare the experiences of old and young women. A woman of 35 or more is certainly old to have her first baby. Between 15 and 25, patients are in the first ten-year period of their child bearing years. So if you compare the old group with the young group, you get a fairly good idea of the hazards to those women who get pregnant in the third period of their child bearing years. We took, year by year, the same number of young primiparas to compare with this group of 312 elderly primiparas from a group of over 25,000 cases from 1938 to 1941. In the elderly group, 116 were 35 years of age; 64 were 36 years old; 43 were 37 years old; 34 were 38 years of age; 28 were 39 years old; 11 were 40 years old; 7 were 41 years; 7 were 42 years; 1 was 43 years old; and 1 was 47 years.

To record duration of labor, we grouped these young and old primiparas into 4-hour periods, up to 24 hours, and then into 6-hour groups to 42 hours. The remainder varied from 42 to 60 hours and over, with the time of labor unrecorded in 53 cases. Although 312 cases represent a small group from which to draw conclusions, nevertheless we could find no really significant difference in the hours of labor between the elderly and the young primiparas.

As far as the weight of the babies is concerned, we took all the babies under 2,500 grams, those from 2,500 to 3,500, which would be approximately in the normal range of birth weight, those from 3,500 to 4,000, and those over 4,000 grams. In the group between 2,500 and 3,500 grams there were 172 elderly primiparas and of the young primiparas, 180. This represents no significant difference.

We considered toxic conditions of pregnancy, and found that the elderly primipara, had a toxemia incidence almost three times as great. Twenty-nine of the elderly primiparas had eclampsia, hypertension, pre-eclampsia and nephritic type of eclampsias, as compared to 10 in the young primiparas.

There were 15 cases of fibromyoma uteri in the elderly primiparas and none in the young primiparas, as would be expected. Heart disease occurred 10 times in the elderly primiparas as compared to twice in the young group. Abruptio placenta occurred about equally in both groups, 7 and 6 respectively. Placenta previa occurred 4 times in the older group and never in the younger group. Postpartum hemorrhage was approximately the same, there being 7 in the older group and 10 in the younger group.

In our women we found no essential difference between the two groups with respect to soft part dystocia. The operative experience of these women was certainly different and I think for good reason. Low forceps was employed about the same number of times for both groups. Midforceps are used about two and a half times more often in the elderly than in the young primiparas.

We had almost the same percentage of cesarean sections in our group as was shown here, 42 of the low, transperitoneal laparotrachelotomy type, and 17 extra-peritoneal sections, a total of 59 in the elderly primiparas as compared to 7 in the younger group. Of these 5 were low flap and 2 extraperitoneal.

The morbidity rate was about twice as great in the elderly primiparas as in the young primiparas.

There were 245 live babies in the elderly primiparas as compared to 292 in the young primiparas, but the premature nonviable infants in the elderly primiparas were much higher.

Our cesarean incidence is comparable to that reported here this evening. It is high but I think rightly so. There are other factors in elderly primiparas more important than their age. When these patients over 35 come to us pregnant for the first time, some of them married for many years, the baby assumes a social importance that is in no way comparable with the baby of a young healthy primipara. The loss of a first baby in a woman of 35 is a real tragedy for it may be her only child. The concurrent fact that she is more subject to the hazards of degenerative diseases of the last third of her childbearing life makes this pregnancy in this patient more likely to be terminated by cesarean section.

Dr. Johnson's figures certainly show the hazard of classical section. I think those three deaths from peritonitis and sepsis, and 1 following the low flap operation might well have been eliminated by different choice of operation. In our series there were 42 low flap and 17 extraperitoneal sections done on elderly primiparas with no deaths. In the young primiparas we did 2 extraperitoneals out of 7 sections, and those were infected and bad risks.

In the entire group of 312 elderly primiparas we had 2 deaths, 1 from cardiac disease before leaving the hospital, and 1 from pulmonary embolism. There were no deaths in the section group. I think that one might stress the importance of not doing any classical sections on any women, and secondly on any potentially or actually infected woman, choose an extraperitoneal rather than a low flap operation. In more than 400 extraperitoneal sections on potentially and frankly infected women, we have had only 4 deaths in the last 10 years.

DR. WILLIAM S. SMITH.—The elderly primipara is a hazard during pregnancy and labor. I believe such a patient should be very carefully considered as to whether she is physically sound and, secondly, as to the probabilities of her being able to withstand a pregnancy and labor.

All elderly primiparas require more rest and more careful watching during pregnancy and labor than is required by younger patients. The obstetrician must be constantly on the watch for early symptoms which may indicate that the pregnancy load is too heavy.

I prefer not to induce labors in these patients before term because such induced labors are often long and difficult. If, after a six- or seven-hour test of labor, a long and difficult labor is probable, a cesarean section should be done at once while the patient is in good condition to withstand the operation.

DR. MEYER ROSENHOHN.—Dr. Johnson's statement in his last paragraph gives his basic conclusion: no cesareans for elderly primigravidas as such, but the presence of any complications or any associated factors which would endanger the life of the baby, warrant this operation. I agree with this. Dr. Smith puts it properly in allowing these patients a test of labor of four to six hours, although I do not subscribe to such a definite period. I should like to refer to two patients we had at the Bronx Hospital who come in this category.

1. A patient, 42 years of age, due December 10, last was admitted November 2, with a history of eight miscarriages, only one of which occurred as late as the seventh month. She had a basal metabolism of plus 40 and exophthalmos. The baby was a fair size ($7\frac{1}{2}$ pounds). She had a polyhydramnios and with the fear of a monstrosity, no cesarean was done. The membranes ruptured spontaneously the next day and after some forty hours, she delivered a healthy, normal baby spontaneously.

2. This patient was the first to introduce me to a term which many of you have undoubtedly heard before, "The change of life baby." She was 44 years of age, married twenty-seven years, and had had an ectopic eighteen years before. She was due August 25, and was found to have a baby which was not large. The matter of cesarean section was explained to her and she was willing to take some of the responsibility. After some forty hours, a midforceps was done and a living normal baby weighing 6 pounds, 10 ounces was obtained. In both these cases the operations, if done, would not have been criticised, and yet both patients were delivered of normal babies per vaginam with no difficulty.

DR. JOHNSON (closing).—There are few problems which offer a greater challenge to the judgment of the obstetrician than that of managing the elderly primipara. The increased value placed on a live infant might cause one to be radical, but we must bear in mind the fact that with radical treatment the maternal organism is undoubtedly subjected to an increased risk. We feel that if more attention is paid to some of the factors outlined, the results in this small, but important, group of patients will be improved.

THE POSSIBLE SIGNIFICANCE OF VAGINAL SMEARS IN THE DIAGNOSIS OF CERTAIN DISTURBANCES OF PREGNANCY*

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AS EARLY as 1917, Stockard and Papanicolaou¹ described the technique of the vaginal smear in studying the estrous cycle of the guinea pig. More recently (1933) the latter² studied the cyclical changes in the human vagina with changes in the endometrium. His monograph in the *American Journal of Anatomy*, May, 1933, is monumental, and includes the changes in the vaginal spread or smear not only during the different phases of the menstrual cycle, but also during pregnancy and the puerperium. The earlier work of Stieve in connection with the changes during pregnancy (1925) is quoted by Papanicolaou in his classic.

In relation to these studies in the histology of the human vagina, many interesting and fascinating developments in the endocrinology of the female reproductive system have occurred. The discovery of the typical estrous reaction of the vagina of rodents by Papanicolaou and Stockard, Long and Evans, and Allen and Doisy made possible the qualitative and quantitative determination of estrogenic hormone. This was followed by the demonstration by Aschheim and Zondek of female sex hormone in the Graafian follicle, placenta, and later in the urine of pregnant women. Subsequent to this came their discovery of large amounts of gonadotropic hormone in urine of pregnant women, with the well-known pregnancy test. Out of the classical experiments of these workers came the essential facts that the follicle or estrogenic hormone stimulates the vagina, and the gonadotropic hormone, the ovary (corpora lutea).

While the Aschheim-Zondek test and the more recent modification of Friedman are based on gonadotropic reaction, the vagina of the rodent has not been given up as a criterion for pregnancy reaction. Zondek has developed a pregnancy test for mares based on the estrous reaction of the vagina of the rat. Mazer³ employs the estrin test alone or in conjunction with the Friedman test for the diagnosis of early pregnancy. He uses the castrated adult female mouse, and his criterion for a positive test is finding a preponderance of non-nucleated epithelial cells and the absence of leucocytes and mucus.

Interest in the pregnant woman from the endocrine point of view has not ceased with the diagnosis of pregnancy.

*Read at a meeting of the Baltimore Obstetrical and Gynecological Society, November 12, 1943.

In 1933, Spielman, Goldberger, and Frank,⁴ realizing that neither the Aschheim-Zondek nor Friedman test can be used to determine the question of the life or death of the fetus (because of the presence of active chorionic tissue after fetal death), utilized the blood estrin levels as an indicator of whether the fetus is alive or dead. These investigators report that beginning at the middle of the second month, the estrin titer constantly increases (the source of the hormone being the placenta). They found a reduction in the blood estrogenic factor within 24 hours after fetal death. More recently, Goldberger and Frank⁵ found that the seventeenth week of pregnancy is the point at which typical pregnancy levels of estrogen begin, and that from then on there is a progressive increase to the end of pregnancy. In their earlier article, they claim that the Frank-Goldberger estrin determination is more sensitive than the pregnancy tests based on gonadotrophic hormone.

The quantitative estimation of pregnancy hormones in the blood and urine of pregnant women was utilized by Smith and Smith⁶ in 1935 in studying toxemias of late pregnancy. They found excessive amounts of prolan and subnormal levels of estrin to be typical of the late toxemias. Similarly, Anselmino in 1936,⁷ performed experiments tending to confirm observations previously made by Heim that in hyperemesis there is an increased excretion of prolan. It has also been shown that excessive amounts of pituitary gonadotropin depress the production of estrogen, and vice versa.

In all these far-reaching advances in endocrine research, the reaction of the patient's vaginal mucosa, that is, the vaginal smear of the patient herself, was not utilized until Papanicolaou and Shorr in 1935 and 1936⁸ demonstrated the changes in the smear of a menopausal patient treated with estrogenic hormone. The menopause, with its sudden and dramatic alteration in reproductive physiology and its attending quantitative hormonal changes, furnishes an ideal laboratory for the study of the vaginal smear. Therefore, the menopause has been the subject of widespread study in this field of research.⁹ And yet, the condition in which modern endocrinology had its birth, namely pregnancy, remains unexplored, insofar as concerns the study of the vaginal smear beyond the strictly anatomic phase, as performed by Papanicolaou and Stieve. With their work as a basis, and making use of the improvements in staining technique of Shorr,⁹ Geist and Salmon,¹⁰ and others, the vaginal mucosa of the pregnant woman deserves the most painstaking study for the detection of variations from the normal, leading possibly to important clinical interpretations. Beginning with the very diagnosis of pregnancy itself, why could not technique be so refined that the simple taking of a smear on the patient would suffice to settle the question? Bearing in mind the quantitative changes in blood estrin levels found by Frank and Goldberger, it is not illogical to suppose that the life or death of the fetus could be determined by the vaginal smear. If the toxemias have a hormonal basis (as many now believe), may we not have a means through the vaginal smear of detecting a toxemia before the usual clinical signs appear, and also of differentiating one type of toxemia from the other? Perhaps, some day soon the vaginal smear may reveal what an eye ground now portends. The question of abortion from blighted ovum or other cause (a subject in which Rutherford¹¹ has become so interested as to perform biopsy on the decidua) might be answered by the vaginal smear. Even if it were not possible to attain the ultimate, such as the afore-mentioned, it would be a great step for-

ward to add to our clinical tests a simple procedure that would correlate certain disturbances of pregnancy with the histology of the vagina.

Papanicolaou, it will be remembered, made no effort to identify a histologic picture with any disturbance of pregnancy. His observations were made apparently from normal pregnancies of known periods of gestation, an anatomic study. Very few individuals to date have endeavored to correlate the vaginal smear of pregnancy with a definite clinical entity. Fletcher¹² (1940) studied the histomorphology of the vagina with special reference to changes observed in cases of incomplete abortion. Using the staining methods of Papanicolaou with modifications, he found certain details in his smears that he suggested might be characteristic of incomplete abortion. Greenhill mentions, in the 1942 Year Book of Obstetrics and Gynecology, a study by M. R. Cohen and B. B. Rubenstein,¹³ reported before the Chicago Gynecological Society in November, 1942, in which vaginal smears were taken and studied in 500 consecutive patients, including pregnant and nonpregnant women. These workers state that the smear in pregnancy is sufficiently typical as to distinguish pregnancy from nonpregnant states. They succeeded in diagnosing pregnancy in 84 per cent of 200 "unknowns." M. J. Bennett and P. B. Russell, Jr.¹⁴ (1941) included in the examination of 15,000 slides some vaginal smears of female fetuses as early as 18 weeks' gestation and corresponding smears in the mothers. They show that the fetus exhibits a follicular stimulation until birth, which gradually decreases until the baby is 94 days old, when it disappears entirely. At 7 months' gestation, the maternal smear shows a predominant follicular influence. The same authors and L. C. Ramsey¹⁵ (1941) studied the vaginal smears in 50 women throughout pregnancy, together with blood estrogen studies, basal metabolic rates, etc. They found close agreement between pregnancy and the normal menstrual cycle.

Grossly, changes in the human vagina as a result of pregnancy have been observed to an extent more exaggerated than the usual textbook description of mere lengthening and increased vascularity. The most striking illustration of anatomic adaptation of the vagina to pregnancy occurred in a patient of the author thirteen years ago.

A recently married young woman consulted me quite disturbed because a gynecologist had just told her she could never have a child except by cesarean section, as her vagina was poorly developed. On examination, I found the vagina stenosed in its middle third, an hour-glass type of stenosis, so that one finger could not get all the way through to the posterior portion. Any attempt to stretch the stenosis was attended by a mild degree of shock. Despite the warning of the gynecologist, I advised the patient to get pregnant, and see "what Nature would do." She promptly conceived, and I examined the vagina at regular intervals throughout the pregnancy. In the early months, very little change could be detected, but at the end of the second trimester definite softening and dilatation of the stenotic portion was apparent, and at about 7 months' gestation, to my great satisfaction and that of the patient, the stenosis had spontaneously corrected itself about 75 per cent, and before labor, about 90 per cent. The result was that the patient delivered per vaginam with the aid of low forceps. The stenosis was permanently cured, and a second pregnancy was uncomplicated by that condition.

This incident impressed me more and more as female endocrinology and reproductive physiology were revealed, for here was a perfect

example of the maturing effect of hormonal stimulation by the high estrogen level of pregnancy on the development of the vagina grossly. Had this case occurred more recently, it would have been possible by the vaginal smear technique to demonstrate the hormone effect histologically.

Histologically, the vaginal mucosa in the normal adult female consists of stratified squamous epithelium of considerable thickness. There is (1) a basement layer of cells known as the basement membrane, next to which is (2) an inner basal zone of small round cells with fairly large nuclei; then (3) a thick layer, known as the functional layer, with larger cells and more varied in shape; and finally (4) a superficial cornified layer, consisting of large, flat, polyhedral squamous cells with small pyknotic nuclei. In conditions of estrin deficiency, such as the menopause, the mucosa becomes thin due to the disappearance of the functional and cornified layers. The smear shows the deep cells known as "atrophy cells," which are small and round with large nuclei, and the presence of large numbers of leucocytes. On the other hand, in conditions of high amounts of estrin, of which pregnancy would be the best example, maximum proliferation of the epithelium of the vagina occurs. Hence, we find in the smear very large numbers of cornified cells of the superficial layer.

The classical studies of the vagina during pregnancy quoted by Papanicolaou, as mentioned before, are those of Stieve (1925).² He found in early pregnancy active proliferation, the epithelium increased enormously in thickness, reaching a maximum of 450 to 500 microns toward the end of pregnancy against an average thickness of 115 to 300 microns for the nonpregnant condition. There is an increase in the number of cells as well as their size, and in the size of the nuclei. Large cells, either isolated or in groups, appear more particularly in early pregnancy. The cornification is, as a rule, not very pronounced, but in many cases one may find nucleated cornified cells. In later pregnancy, Stieve saw cells of larger size with large nuclei and not as numerous as in early pregnancy. Nucleated cornified cells become more and more rare, but the anucleated eosinophilic cells gain in prominence in late pregnancy, and often occur in large heavy groups. Crowded cells and a high cellular disintegration with liberation of nuclei are often characteristic, according to Stieve.

Material and Results

In order to attempt to correlate the classic histologic studies of Papanicolaou and Stieve on the vagina of pregnancy with the endocrinologic advances of recent years mentioned earlier in this article, the author decided to study a series of vaginal smears in pregnant women. Beginning in January, 1941, each prenatal patient in the obstetrical clinic of the Sinai Hospital had a smear taken by the dis-

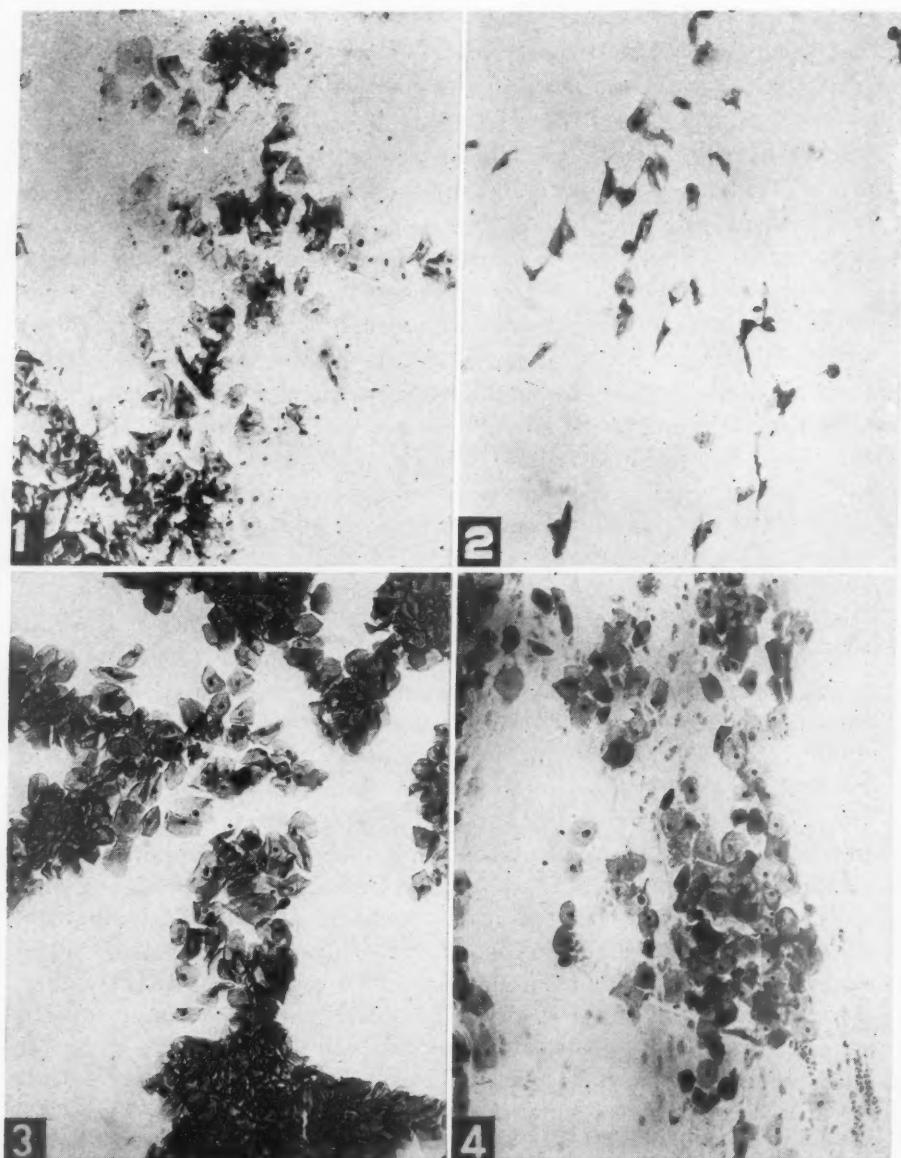


Fig. 1.—Case of normal pregnancy of 3½ months' gestation. Smear typical. Crowding of cells; cells moderately uniform; predominantly large cornified cells with small nuclei. No pus; no "deep" cells.

Fig. 2.—Case of missed abortion. Smear taken at 2 months' gestation. Diagnosis of missed abortion several weeks later. Smear shows no evidence of fresh cornification. Cells elongated and varied in size and shape. No large uniformly shaped cells.

Fig. 3.—Case of hyperemesis gravidarum. Ten weeks' gestation. Smear shows cells intensely eosinophilic. Uniformity in size and shape of cells striking; cells invariably larger than typical. Smear strikingly devoid of other elements, such as pus, mucus, bacteria, etc.

Fig. 4.—Case of early hypertensive toxemia (no vomiting) 4 months' gestation. Smear—Cells are smaller than in Fig. 3, but larger than in Fig. 1. There is not the same degree of uniformity as in Fig. 3.

pensary staff. Instead of the aspiration-pipette method, the technique used was rolling a cotton swab on the lateral vaginal wall. The smears were fixed immediately in alcohol-ether. The stain used was hematoxylin-eosin. About 350 smears were taken, every stage of pregnancy being represented. All smears were examined by the author.

Before going into a description of the smears selected for this paper, it is well to bear in mind that before any judgment can be passed on the value of smears, one must be thoroughly familiar with the normal varia-

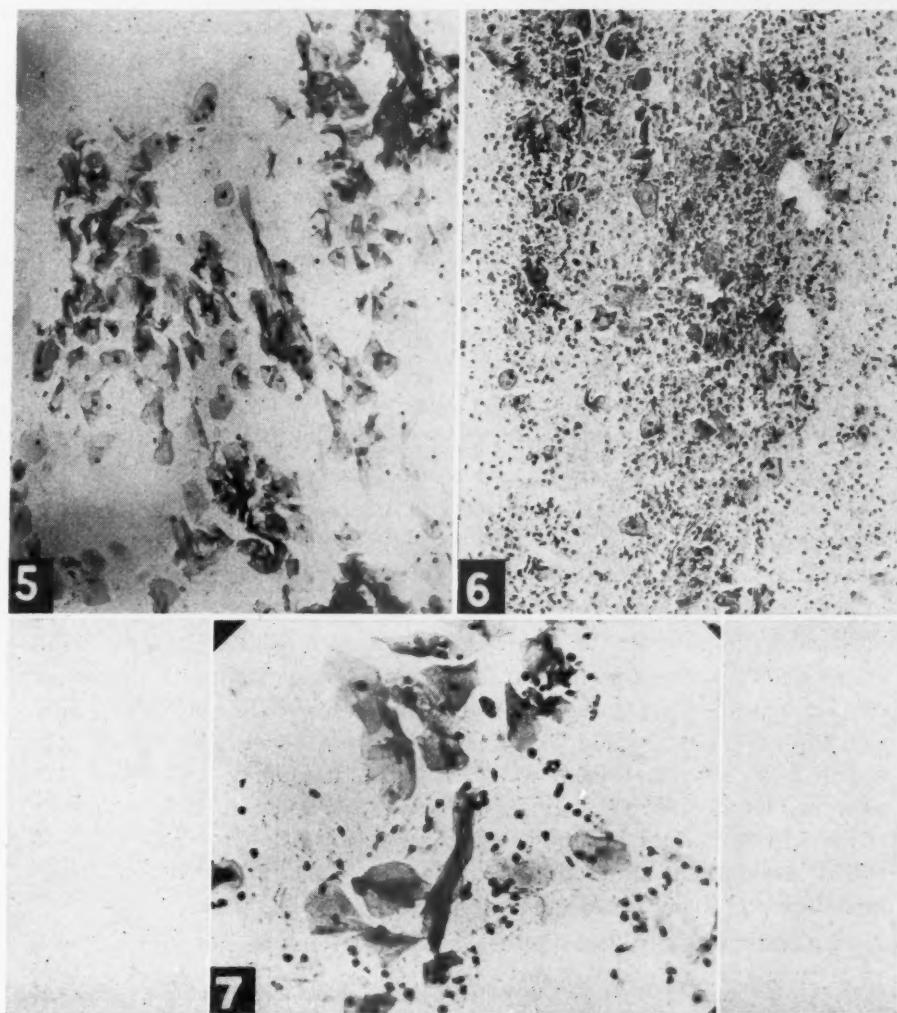


Fig. 5.—Case of normal pregnancy of 10 weeks' gestation at time of smear. Subsequently, patient had symptoms of threatened abortion lasting several weeks. Finally aborted at 5 months. Smear typical of normal pregnancy. (Compare with Fig. 1.)

Fig. 6.—Case of pre-eclamptic toxemia; stillbirth at 8½ months. Smear (taken at 6 months) shows large amount of pus. Many of the vaginal cells are of the deep or basal zone (small round cells with large nuclei).

Fig. 7.—(High power). Case of spontaneous abortion at 3 months. Smear (taken shortly before symptoms of abortion began) shows presence of pus cells. (No red blood cells.)

tions in cellular elements of the vagina. Papanicolaou himself states that no one but an expert in the cytology of the vagina can properly judge or interpret the vaginal smear. It goes without saying that, as a clinician the author cannot qualify in this respect. Accompanying each microphotograph, brief clinical facts are mentioned, so that the disorder of pregnancy can be correlated to the histologic appearance of the smear.

The author has not been able to demonstrate some of Stieve's findings, especially the difference between the smear of early and that of late pregnancy. To the average clinician with limited experience in histopathology, the chief characteristics of the pregnancy smear are the increased size and number of the cells, the presence of large numbers of eosinophilic cornified cells, and the absence of deep cells.

The degree of cornification in a large percentage of smears is so pronounced that it seems possible pregnancy might be diagnosed in this way, excluding nonpregnant states treated with large doses of estrogens. There is one condition which should be readily differentiated from pregnancy by the vaginal smear, namely, the menopause. This can be of great clinical value because of the numerous occasions on which the obstetrician or gynecologist is confronted with the problem of diagnosing a sudden amenorrhea in a 40- to 45-year-old patient.

The highest degree of cornification was seen in a case of hyperemesis. Not quite so marked, but definitely increased amount of cornification was also noted in a case of hypertensive toxemia (early). In a case of pre-eclamptic toxemia, smaller cells with larger nuclei, resembling cells of the basal zone, were seen, suggestive of estrin deficiency. This would go hand in hand with the findings of Smith and Smith⁶ in their blood estrin determinations in the late toxemias. Comparison with the smear of the case of hyperemesis lends interesting speculation as to the relationship of the early and late toxemias. Those who have consistently opposed the neurotic theory of vomiting of pregnancy might find support for an organic etiology in the smears of a series of hyperemesis cases. Investigators on the trail of the toxemias by means of blood estrin levels might study the vaginal smears as a further index of hormonal disturbance in pregnancy.

In a case of missed abortion, fresh cornification was not present; cells were sparse, and appeared shrivelled. While there was no evidence of estrin deficiency, the usual picture typical of the response to pregnancy was not observed. If the vaginal smear could detect death of the fetus before clinical signs of abortion began, it would prove to be a much simpler method than the Frank-Goldberger blood-estrin test.⁴ In a smear taken shortly before a patient had signs of a spontaneous abortion, pus cells were found. On the other hand, in a case where abortion was threatening for some weeks, the smear taken two months before

abortion showed no pus. The interpretation might be made that in the first case a blighted ovum with an abnormal hormonal response caused abortion, whereas, in the latter case, mechanical or local conditions in the uterus itself were responsible. In these two cases and in the case of missed abortion, therefore, we see three different clinical pictures and, correspondingly, three different types of smear. The ability to interpret correctly a vaginal smear in a patient before any bleeding or other symptoms of abortion occur may indeed be of great practical value in cases of habitual abortion where the cause is obscure, and where the physician seeks earnestly to employ rational therapy instead of that of the gunshot variety. For obvious reasons, smears taken after vaginal bleeding has begun are valueless.

A large amount of pus was found two months before a patient delivered a stillborn infant; this case, however, was complicated by toxemia.

In the author's opinion, pus is not a normal component of the vaginal smear of normal pregnancy, if the technique of the cotton swab rolled on the lateral vaginal wall is used. With the pipette method, the vaginal pool is aspirated, containing not only vaginal cells, but secretions of the cervix, such as pus and mucus, as well as microscopic blood from erosions and even from the interior of the uterus itself. Fletcher used the applicator, lateral wall method, but he took smears on women who had already aborted, and therefore he had to contend with blood elements and debris that came in contact with the lateral vaginal wall. It seems logical to state that in order to obtain a vaginal smear approaching the histologic detail of a true biopsy of the vagina, one must eliminate cervical and uterine secretions, and this can be accomplished only by the method described in detail by Fletcher¹² and used by the author.

Summary

Approximately 350 vaginal smears taken on an equal number of patients during all stages of pregnancy were studied, and several smears of cases of different types of toxemias and different clinical varieties of abortion and fetal death are presented, and an effort is made to interpret them based on established hormonal variations in pregnancy, with especial reference to estrin levels. Making use of our constant gain in knowledge of the chemical properties and biological changes in the cells of the human vagina, yet realizing that a high degree of skill in the interpretation of the stained smear is required before widespread clinical application can be attained, it is suggested that histomorphologic patterns can be discovered in certain obstetrical conditions sufficiently clear to warrant the use of the smear as a definite aid in diagnosing and prognosticating disturbances of pregnancy. It is the purpose of this study and the hope of the author to stimulate interest in the use of the vaginal smear in obstetric practice.

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A SUGGESTED PROPOSAL FOR THE CLASSIFICATION OF TOXEMIAS OF PREGNANCY*†

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THE American Committee on Maternal Welfare in 1939 elaborated a classification of toxemias of pregnancy as follows:

Group A. Disease not peculiar to pregnancy:

1. Hypertensive or Arterial Vascular Disease
 - a. Benign {mild
{severe, cardiorenal
 - b. Malignant
2. Renal Disease
 - a. Glomerulonephritis {acute
{chronic (mild or severe)
 - b. Pyelonephritis {acute
{chronic
 - c. Other forms of severe renal disease: Nephrosis, polycystic kidneys, and other congenital anomalies of the kidneys

Group B. Disease dependent on, or peculiar to, pregnancy:

1. Mild pre-eclampsia
2. Severe pre-eclampsia (preconvulsive)
3. Eclampsia

Group C. Vomiting of pregnancy

Group D. Unclassified toxemias

- a. Those patients in whom a definite diagnosis cannot be made to allow them to fall into Group A or B (i.e., glomerulonephritis suspects).
- b. Many will fall into the above-known groups post partum, but insufficient data before or in the early months of pregnancy make it imperative to exclude them from statistical data except when autopsy findings ultimately allow them to be put in either Group A or B.

The best that can be said for this grouping is that it represents an earnest effort toward uniformity in classifying these various conditions for study and thence for treatment. Its outstanding feature seems to be an attempt to divide such women into two groups, the first having recognized pathologic conditions predisposing to the crisis called the "toxemia of pregnancy," and the second embracing women apparently healthy in whom the "toxemia" was precipitated by the pregnancy. I believe that this is indeed weak and faulty, necessarily so because our knowledge of the precipitating causes of these acute conditions is so incomplete.

However, quite apart from such mild and hopeful criticism as this is another, and to me, extraordinary situation in this connection. This

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is that one member of the Committee (Foster Kellogg writing with Duncan Reid a few months after adoption of the Committee's report) undertakes to edit this grouping by deleting vomiting of pregnancy, or *hypemesis gravidarum*, having "taken the stand that *hyperemesis gravidarum* (as well as acute yellow atrophy, previously omitted) is not related to the late toxemias of pregnancy." (See also Smith¹ of the same Boston group.) Apparently these two conditions were dropped because they usually occur early rather than late in pregnancy, even though others that were included, especially under Group A, may become manifest at any time, late or early. This seems to have made this classification more confusing rather than to have clarified it.

It seems even more logical to continue to include nausea and vomiting of early pregnancy as a recognized toxemia of pregnancy, than it does to add chronic pyelonephritis. Yet it is proposed to delete nausea and vomiting but to add pyelonephritis even though the latter is, actually, only an illness possibly predisposing to some of these other disturbances termed toxemias. It would be difficult to convince any woman seriously ill with *hyperemesis gravidarum*, or her family physician, that this is not a toxemic illness of pregnancy.

Those obstetricians who so universally favor the intravenous administration of dextrose solution in eclampsia may be interested to know that my² original suggestion of this for this purpose was directly an outgrowth of our observations on its beneficial effects in severe grades of hyperemesis. The arguments, now so familiar, were so logical and reasonable then in the days when hyperemesis was a toxemia and women still died of it, that they need not be recounted. The general adoption of this therapy and its benefits for both hyperemesis and eclampsia have served to do nothing else than strengthen my belief in the etiologic and clinical relationship of all of these toxic manifestations of early and of late pregnancy.

Criticism such as this would be unwarranted if not supported by a trial and its results. Williams and Weiss³ attempted to tabulate 318 cases of toxemia of pregnancy under this classification, and have the following to say: "The application of this classification to material such as we have studied was not entirely satisfactory." They add, to soften the comment, "this was due in large part to the limitations of some of the material."

Criticism such as I have made would be mere faultfinding if nothing about it were constructive. Williams and Weiss offered suggestions for changes to amplify and strengthen the original classification, and I venture to suggest an entirely new classification which I believe answers most if not all of the objections raised about this other. As a matter of fact, no one knows the limitations of this first classification better than the authors themselves, as they freely announce. (Mussey and

Hunt).⁴ Until our knowledge of the etiology of toxemia is more advanced than it is now, any classification will be incomplete.

The one offered here is, quite frankly, the result of proposals and purposes expressed by the keen minds of that Committee, but it retains the more solid of the older views as to what may be considered by us as toxemias, why they develop, and also this viewpoint of their possible or even probable relationship to each other.

Proposed Classification

Group A. Toxemia types most common early in pregnancy (Nausea and vomiting)

1. With demonstrable pre-existing, predisposing causes (including dietetic, or endocrine, or cardiovascular disturbances, alone or in combinations)
2. Without demonstrable pre-existing, predisposing causes

Group B. Toxemia types occurring without predilection to any time during pregnancy (Acute yellow atrophy of the liver, acute nephritis or other renal disease, acute hypertensive cardiovascular disease, and certain unclassified types)

1. With demonstrable pre-existing, predisposing causes (including dietetic, or endocrine disturbances, or general physical defects), alone or in combination
2. Without demonstrable pre-existing, predisposing causes

Group C. Toxemia types most common late in pregnancy (Pre-eclampsia, and eclampsia)

1. With demonstrable pre-existing, predisposing causes (including dietetic, or endocrine disturbances, or general physical defects, alone or in combinations)
2. Without demonstrable pre-existing, predisposing causes

Unlike the other classification, this one makes pregnancy the common denominator, emphasizes the peculiar groups of symptoms which we have always been accustomed to think of as types of toxemia of pregnancy, and also relegates various predisposing causes for these back to a minor role rather than including any of them as a "toxemia."

It allows for inclusion of most of the current theories as to possible causation, and I cannot find any case in our series that could not be classified fairly satisfactorily under one or another of these tabulations. There may occasionally be some trifling overlapping in classification of a given case, but this is usually readily reconciled.

It allows for the view held by many that each type of toxemia of pregnancy is a separate entity unrelated to the others. It provides equally well for the opposite view, in which I believe so strongly, that there is a basic underlying relationship between all of these types, their outstanding symptoms varying only because of the influence of various modifying factors.

Summary

1. The classification of toxemias of pregnancy proposed by the American Committee on Maternal Welfare has been found unwieldy and unworkable.
2. Its proposal suggests, however, that further attempts be made to devise a suitable classification in order that toxemias of pregnancy may be tabulated in an orderly fashion to permit study of their various general types.
3. A simpler and more inclusive classification is offered for consideration and use in this respect, if found acceptable.

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1015 HIGHLAND BUILDING

INTRAVENOUS ADMINISTRATION OF VINBARBITAL SODIUM* **FOR INDUCTION OF OBSTETRIC AMNESIA**

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THE selection of suitable agents for the production of amnesia and analgesia is doubly important in obstetrics as compared with any other field of medicine. The obstetrician must have continuous concern for at least two patients and any method he employs must produce a specific effect upon one and not upon the other and should not alter the vital processes of either the mother or child. The desirability, and indeed the necessity for inducing amnesia and analgesia during parturition is now universally recognized. Numerous agents and methods have been advanced which are purported to produce the desired effect and to avoid undesirable and dangerous side reactions. The obstetrician must remind himself continuously of certain fundamental requisites demanded of any drug or method employed to induce successful amnesia. These requirements are as follows:

1. Amnesia for pain. Somnolence and amnesia during the intervals are not difficult to induce but severe psychic trauma may be sustained unless complete or nearly complete recollection of pain is obviated. This is particularly pertinent today when most of the laity has been conditioned through popular channels of communication to fully expect "painless childbirth."
2. Maternal respiration and circulation should not be altered or depressed.
3. Labor should not be prolonged.
4. There should be no residual fetal or maternal toxicity (i.e., asphyxia and "hangover" respectively).

Prior to August, 1941, the results obtained by oral administration of vinbarbital sodium were most encouraging. In many instances, however, it was considered desirable and advantageous to employ an agent which would produce amnesia in a much shorter time than that required for any oral preparation. Because of our previous experience and the failure to observe any significant side reactions or alteration of blood pressure and respiration when vinbarbital sodium was given orally, it was suggested that this drug be prepared in a manner suitable for intravenous administration.

A preparation of vinbarbital sodium which could be given intravenously was provided during the summer of 1941, and from September of that year to May, 1943, obstetric amnesia was induced in 1,500 consecutive patients with this agent. The results observed in the last series,

*Vinbarbital sodium is the nonproprietary name for sodium 5-ethyl 5-(1-methyl-1-butenyl) barbiturate, and is distributed under the name of "Delvinal" Sodium. The material used in this study was provided through the courtesy of Sharp & Dohme, Philadelphia, Pa.

consisting of 296 patients, have been subjected to a critical analysis and are contained in this presentation. The remainder of the consecutive series of 1,500 patients was similar in all respects to the one herein presented and was omitted only because of lack of time and personnel required for the detailed presentation of such a large survey.

The pharmacologic and clinical attributes of this drug, when administered orally, have been favorably reported upon by competent investigators.¹⁻⁶ The intravenous preparation is a solution of 1 gr. of vinbarbital sodium per c.c. in propylene glycol and distilled water. A standardized method for induction and maintenance of obstetric amnesia was established for the purposes of this study and administered to all patients during the course of the present investigation as follows:

Method

When uterine contractions were noted at regular intervals of seven minutes or less, 3 to 5 gr. of vinbarbital sodium were administered intravenously over a period of approximately one minute. Immediately following the intravenous administration of vinbarbital sodium $\frac{1}{130}$ gr. of hyoscine hydrobromide was injected intramuscularly. If delivery had not occurred within forty-five minutes, $\frac{1}{260}$ gr. of hyoscine hydrobromide was administered intramuscularly and this dose was repeated in another forty-five minutes. Thereafter, $\frac{1}{260}$ gr. of hyoscine hydrobromide was administered intramuscularly at ninety-minute-intervals as necessary to maintain amnesia. All patients were delivered under gas-ether anesthesia with the aid of prophylactic forceps, or by simple extraction if the breech presented.

Within twenty-four hours post partum, each patient was questioned closely concerning her subjective reaction to the method employed for production of amnesia and analgesia. The replies from 1,500 patients to whom the above outlined method was administered were as follows:

1. Complete amnesia, 90 per cent
2. Partial amnesia, 8 per cent
(recollection of isolated events)
3. No amnesia, 2 per cent

Results

The objective findings were equally encouraging. No noticeable change occurred in maternal blood pressure, or in the cardiac or respiratory rates. This is in marked contrast to our previous experience with another barbiturate administered intravenously which produced a high percentage of maternal respiratory depression. The fetal heart sounds were unaffected. There was no slowing or interruption in the progress of labor. In a number of instances induction of amnesia, with vinbarbital sodium was started early in labor with deliberate intention to determine whether or not administration of this drug would interrupt or slow the progress of labor. No tendency for any delaying

activity was ever observed. The incidence of post-partum hemorrhage was 2 per cent which was practically identical with that currently observed in patients on other obstetric services and regardless of the fact that sedation had or had not been employed. There was no mental depression (disorientation or "hangover") after delivery with the exception of one patient whose past history revealed unusual susceptibility to barbiturates. It was necessary in approximately 30 per cent of patients to resort to some mild application of restraint. This was soon discovered to be a hyoscine effect and not produced by vinbarbital sodium, since it occurred when hyoscine was administered alone. A study is now under way to reduce or eliminate the restlessness caused by hyoscine. There were no cases of fetal asphyxia even though vinbarbital sodium was administered within a very short time prior to delivery. After experience with the drug had reached considerable proportions, amnesia was induced deliberately with vinbarbital sodium in a number of patients who were known to be within minutes of delivery. In no instance was asphyxia or delayed respiration noted and 8 of these patients delivered in thirty minutes or less (2 at nineteen and seventeen minutes respectively) following the administration of vinbarbital sodium.

The pertinent details of the case histories of the 296 patients presented in this report are as follows: There were 183 primiparas or 61.8 per cent, and 113 multiparas or 38.2 per cent. In 284 patients (95.9 per cent) delivery was completed within twelve hours subsequent to induction of amnesia. Delivered from this group of patients (296 mothers) were 285 living infants (1 pair of twins). In addition there were 5 fetuses of two to five months intrauterine age, 3 monstrosities and 2 macerated stillborn infants of seven and eight months respectively. There were also 2 full-term stillborn infants delivered; one from a mother whose diabetes mellitus had been difficult to control throughout pregnancy and who died shortly after parturition; and one from a mother who had an unusually difficult labor of one hundred ten hours and in whom a cesarian section or other operative intervention was contraindicated. In the group of 285 living infants, there were 3 who were born prematurely. A conservative estimate of their average intrauterine age was approximately seven months. These infants were delivered two, four and a half and five and three-quarter hours respectively, subsequent to induction of amnesia with the intravenous preparation of vinbarbital sodium. There was no delay in establishment of respiration.

In this group also there were 8 living infants delivered by means of cesarean section. One child was delivered in this manner fifty-two minutes after vinbarbital sodium was administered to the mother. The time between administration of the drug and the delivery of the remaining 7 infants ranged from three to nineteen and a half hours. No deleterious effect attributable to the drug was noted in the mothers or infants.

In Group I, fifty-one mothers completed the second stage of labor within one hour of administration of vinbarbital sodium intravenously. Of these 21 were primiparas and 30 were multiparas.

Forty-eight living infants were delivered in this group among which are included one child delivered by cesarean section and a pair of twins delivered through the natural birth canal. There were 2 macerated stillborn infants whose intrauterine ages were calculated at seven and eight months respectively, and also 2 monstrosities.

In Group II, the second stage of labor was completed by 60 mothers in less than two hours, but more than one hour, after intravenous administration of vinbarbital sodium. Of these 25 were primiparas and 35 were multiparas. Sixty living infants were delivered in this group of which 1 child was born prematurely at approximately seven months.

In Group III, 70 mothers completed the second stage of labor in less than four, but more than two hours, after the intravenous dose of vinbarbital sodium. Of these 40 were primiparas and 30 were multiparas. Sixty-eight living infants were delivered among which are included 2 delivered by cesarian section. Two mothers delivered fetuses of approximately two and a half to three months intrauterine age.

The remainder of the series of 296 mothers, or 115 in Group IV, completed the second stage of labor four hours or more after vinbarbital sodium was administered intravenously. Only 12 mothers in this group failed to complete the second stage of labor within twelve hours. The average time of delivery of 103 mothers was approximately eight hours following intravenous administration of vinbarbital sodium. From this group of mothers 109 living infants were delivered among which are included 2 prematurely born babies of approximately six and a half to seven months intrauterine age and 5 infants delivered by caesarian section. There were 3 fetuses of two, four and five months respectively; one monstrosity and 2 full-term stillborn infants mentioned previously.

TABLE I. SUMMARY OF DATA

PATIENTS	ENTIRE SERIES	GROUP I*	GROUP II*	GROUP III*	GROUP IV*
Primiparas	183	21	25	40	97
Multiparas	113	30	35	30	18
Total	296	51	60	70	115
Living infants	285	48	60	68	109
Premature	3	-	1	-	2
Cesarean section	8	1	-	2	5
Stillborn	9	2	-	2	5
Monstrosities	3	2	-	-	1

*Group I.—Delivery occurred one hour or less after induction of amnesia.

*Group II.—Delivery occurred within two hours but more than one hour after induction of amnesia.

*Group III.—Delivery occurred within four hours but more than two hours after induction of amnesia.

*Group IV.—Delivery occurred four hours or more after induction of amnesia.

Summary and Conclusions

- Observations made on 1,500 consecutive patients and a study of the results obtained in the last 296 patients of this series, indicate that

vinbarbital sodium is an effective preparation for induction of obstetric amnesia and is without harmful effects to mother or child.

2. Complete amnesia was obtained in 90 per cent of the series of 1,500 consecutive patients to whom vinbarbital sodium was administered intravenously. Only 2 per cent of patients so treated failed to obtain amnesia and 8 per cent were able to recall isolated events.

3. Administration can be accomplished rapidly, and amnesia is obtained within ten minutes or less after injection.

4. In all instances patients were able to cooperate and respond to necessary requests during the course of labor. The induction of general anesthesia proceeded smoothly and did not precipitate any mental excitement or undue motor activity.

5. The contractility of the uterus was unaffected by vinbarbital sodium as evidenced by the following observations:

- a. There was no interruption or slowing of the progress of labor even when the drug was administered early.
- b. The incidence of post-partum hemorrhage was not increased over that usually encountered in this area.

6. No alteration in the vital functions of mother or child was observed during the first stage of labor regardless of the interval of time between administration of the drug and the onset of the second stage.

7. No mental depression was observed after delivery. The patient awakened from a refreshing sleep with no disorientation or "hangover."

8. In the entire series there was no case of fetal asphyxia or fetal death that could be attributed to the effects of the drug.

9. The intravenous use of vinbarbital sodium in this large series of cases has proved to be a most satisfactory preparation for induction of obstetric amnesia and has been found to meet all the requirements demanded of any drug employed for this purpose as set forth at the beginning of this presentation.

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CONGENITAL VAGINAL OCCLUSION OF THE CERVIX*

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TWO years ago a young woman presented herself because of sterility and incidental menorrhagia. On examination there was an apparent congenital absence of the cervix with an imperforate vaginal vault, which from the embryological viewpoint seemed to be an impossible malformation. Recently a second patient, who consulted me because of severe dysmenorrhea, was found to have essentially the same developmental defect. These two cases had so many similar features that it seems logical to discuss them together.

CASE 1.—R. S., aged 21 years, consulted me in January, 1942. She began menstruating at 13, and always had a painless and regular flow, lasting from eight to ten days. She had been married for two years and complained chiefly of sterility and frigidity, although during the previous few months there had been a little postmenstrual staining. The external genitals were normal. The configuration and size of the vagina were normal except for the apparent absence of the portio of the cervix in the vaginal vault. This area looked as though the patient had been subjected to a total hysterectomy. On bimanual examination a small uterus, deviated to the right, with normal adnexa could be palpated in the pelvis. After putting the vaginal vault on the stretch with a bivalve speculum, and making a careful search, a small pin-point opening in the center of the vaginal vault was seen (Fig. 1). This was not large enough to accept an ordinary uterine sound, nor even a fine wire probe. A bougie tip No. 5 ureteral catheter was then inserted through this small opening but was arrested at 3 cm. One week later I cut off the end of this catheter, reinserted it through the tiny opening, and took a series of salpingograms, using fractional injections of lipiodol, as suggested by Hyams. These pictures revealed an apparent pocket just above the vaginal vault, with a small diverticulum on each side, above which there was a dilated cervical canal and a small dextroverted uterus (Figs. 2 and 3). The contrast medium failed to demonstrate any tubal patency on the right side, but showed a long tube on the left side with apparent retention of the oil in the fimbriated extremity. The twenty-four-hour picture, however, demonstrated small flecks of oil scattered in the pelvis, so it was evident that the tube on the left side was open (Fig. 4). Five months later I attempted to circumcize the vaginal vault and mobilize the cervix, but after completing this operation was entirely dissatisfied with the end result, as I had not been able to find any anatomic landmarks or definite lines of cleavage. Four months after this plastic procedure, in October, 1942, the patient became pregnant and went through a normal pregnancy under the supervision of her family

*Read at a meeting of the New York Obstetrical Society, February 8, 1944.

physician. She was delivered of a seven-pound baby by a general surgeon, who did a classical cesarean section in August, 1943, and had a smooth post-partum convalescence. When I re-examined this patient two months later, the vaginal vault still presented much the same appearance

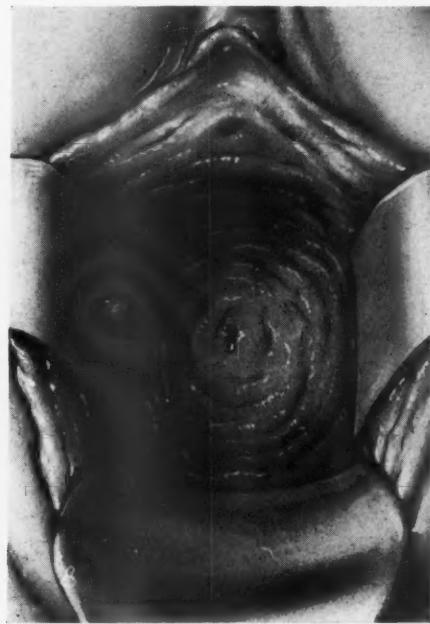


Fig. 1.—(Case 1.) Apparent congenital absence of the cervix, with small opening in the center of the vaginal vault.

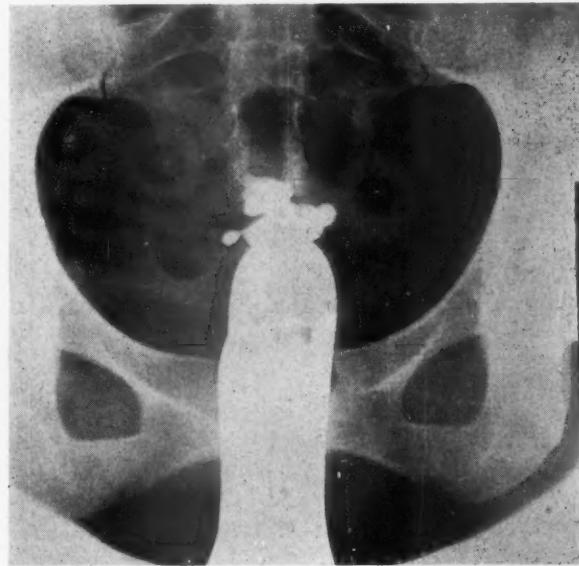


Fig. 2.—(Case 1.) Injection of 2 c.c. of lipiodol, showing a pocket between the vagina and cervix with a small diverticulum on each side.

as when she was first seen, except for the fact that the epithelial covering of the area in which the cervix normally lies looked much like the surface of a cervix which had been subjected to a partial amputation. There was just a little difference in the smoothness of the mucous membrane covering this area contrasted with the rugae in the rest of the vaginal canal.

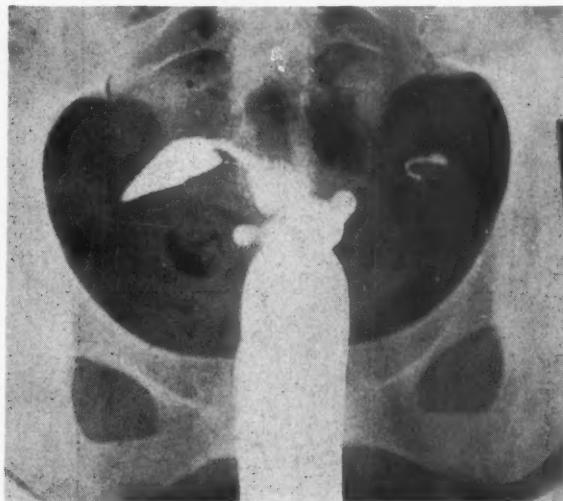


Fig. 3.—(Case 1.) Injection of 10 c.c. of lipiodol, showing the rugae in the dilated cervical canal, marked dextroversion of the uterus, right tubal occlusion at the uterine cornu, and apparent tubal occlusion of the left tube at the fimbriated extremity.

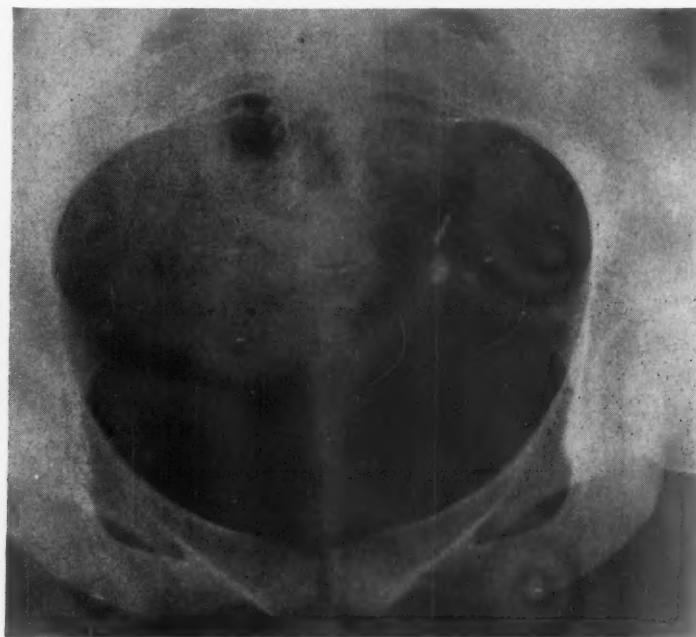


Fig. 4.—(Case 1.) Twenty-four hours after lipiodol injection, showing flecks of contrast medium in the left iliac fossa, indicating patency of the left tube.

Unfortunately, this patient could not be persuaded to submit to additional salpingograms after delivery.

CASE 2.—J. R., aged 22 years, consulted me in August, 1943, because of severe and increasing dysmenorrhea, with slight menorrhagia. She began menstruating at 11, and usually flowed rather profusely for six days, at two-week intervals. While there had always been some pain with the flow, the dysmenorrhea had been increasing in recent months. She had been married for a year and a half before seeking medical advice. On examination this patient's vaginal vault was found to resemble exactly the one described in the first case, except for the fact that no opening could be found in the midline. After prolonged search, a tiny opening was found far over on the left side (Fig. 5).

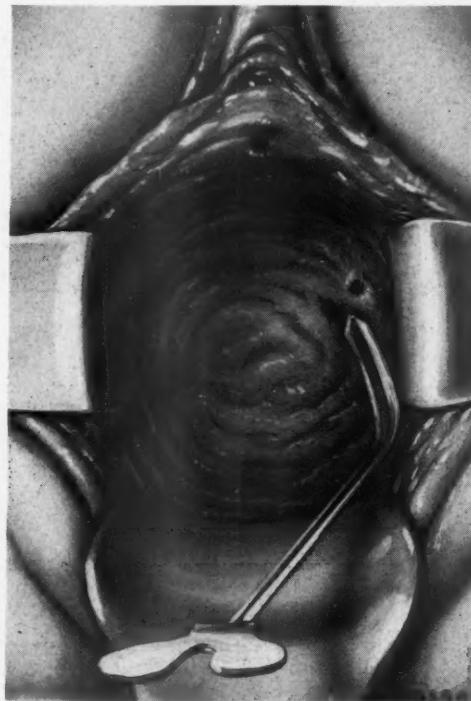


Fig. 5.—(Case 2.) Grooved director pointing to small aperture in left side of the vaginal vault.

This aperture accepted an ordinary silver probe without difficulty. The probe could be inserted for about seven em., and could be moved around to a certain extent. On bimanual examination a cervix and uterine corpus could be palpated in the midline, with a normal tube and ovary on each side. Salpingograms in this instance, which were also made by using a ureteral catheter tip, disclosed a large blind pouch only, and none of the contrast medium entered the cervical canal, uterine cavity, or tubal lumena (Figs. 6 and 7). In October, 1943, a malleable grooved director was inserted into the opening with its tip curved to the right and the mucous membrane of the vaginal vault was split transversely with a knife blade on the grooved director (Fig. 8). The tissue, which was cut through by the knife blade, looked like normal vaginal

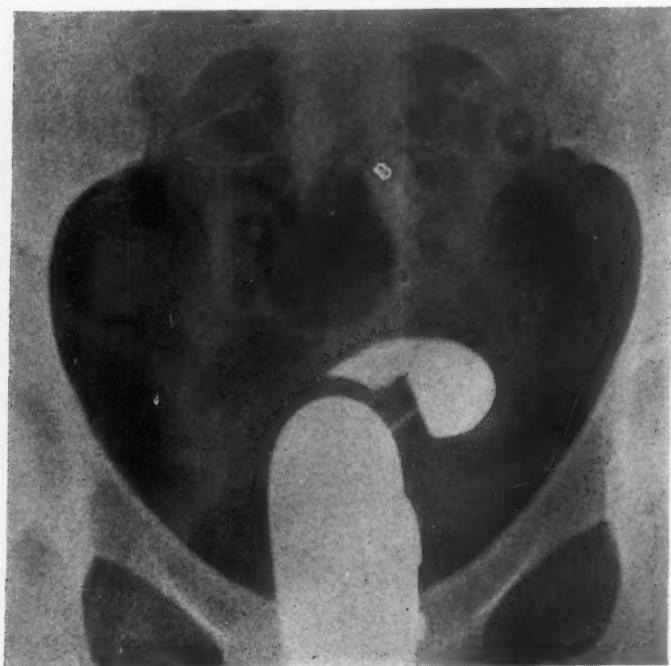


Fig. 6.—(Case 2.) Injection of 2 c.c. of lipiodol, demonstrating large supravaginal pocket.

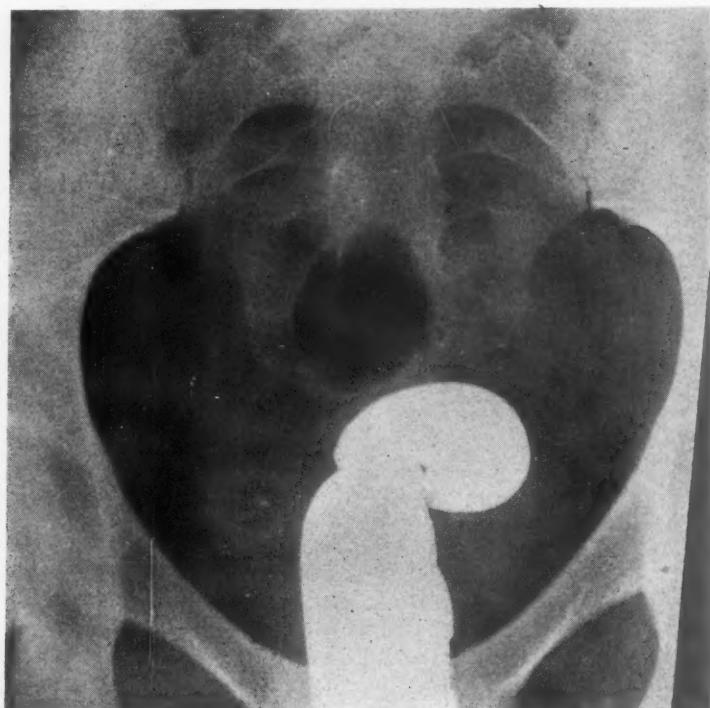


Fig. 7.—(Case 2.) Injection of 10 c.c. of lipiodol, distending the pocket and disclosing no evidence of a uterus.

mucous membrane of average thickness and, as the incision was made, the margins retracted anteriorly and posteriorly, permitting the escape of a large quantity of gelatinous mucus, with delivery of a fully-developed cervix into the vagina (Fig. 9). The cervix was normal in every respect except for a large area of erosion surrounding the external

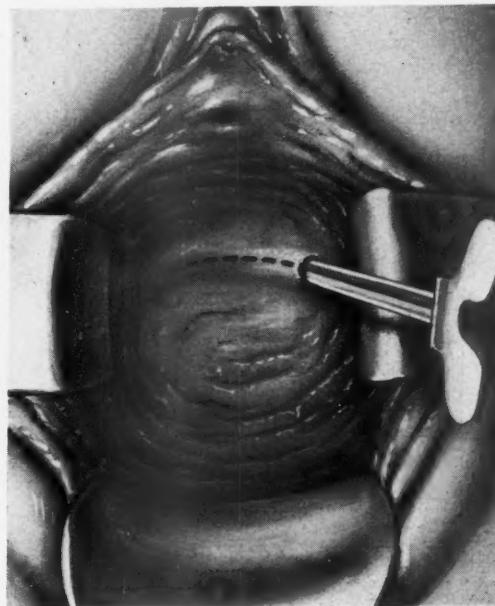


Fig. 8.—(Case 2.) Showing line of transverse incision of vaginal vault mucous membrane.

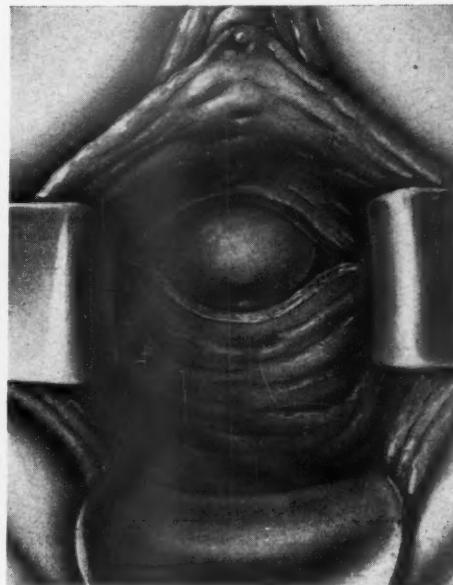


Fig. 9.—(Case 2.) Exposure of normal cervix after incision.

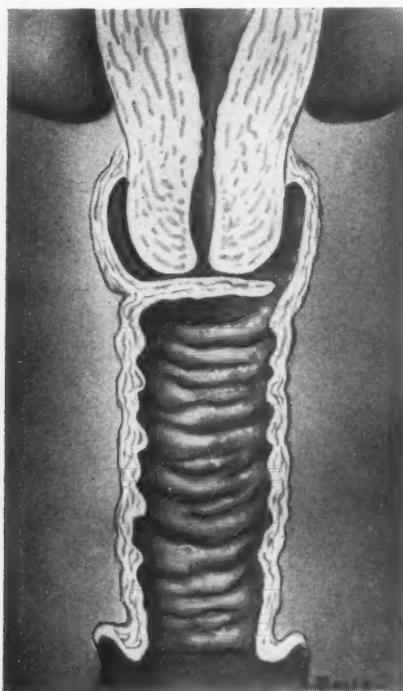


Fig. 10.—(Case 2.) Diagrammatic depiction of the uterovaginal anomaly.



Fig. 11.—(Case 2.) Salpingograms taken 2 months after operation, demonstrating a normal uterus and tubal patency.

os. A uterine sound was easily inserted into the uterus for a distance of three inches, and the endometrial surface was curetted with a semisharp curette. It then became evident that this patient had a normal uterus and adnexa, but that the cervix had been completely occluded by a transverse partition of vaginal mucous membrane (Fig. 10). After two normal and painless menstrual periods following the operation, another series of salpingograms was made, by injecting lipiodol through a cannula inserted into the newly exposed cervix. These pictures demonstrated a well-developed uterus and bilateral tubal patency (Fig. 11).

Comment

The first mysterious feature of these two cases is the developmental origin of the transverse occluding membrane in the upper vagina which concealed the cervix. How the Müllerian duct development was distorted to create the occluding transverse partition in the vaginal fornix is an enigma. Robert Meyer believes that most vaginal occlusions at the introitus are acquired by inflammatory processes presumably caused by infectious diseases of childhood. Perhaps this theory could be accepted in the first case, but it hardly seems applicable in the second one, because the vaginal vault tissue was too thick and in no wise differed from the rest of the vaginal mucosa. The second peculiarity which is difficult to explain in both cases is the presence of the miniature openings in the obstructing partitions, one in the center and one far on the left side. They had no direct continuity with the cervical canal in either instance, yet provided a means of egress for mucus and menstrual blood through the false pouch between the cervix and vagina. The original salpingograms demonstrated that the ureteral catheter tip did not enter the cervical canal in either patient, and the filling of the endometrial cavity in the first case seems to have been due to little more than good fortune. The subsequent pregnancy was an agreeable surprise, especially because of the tubal occlusion on one side and questionable patency on the other. It is a matter of regret that the operator did not do a low flap section, which would have permitted inspection of the cervical region after detachment of the bladder.

The disclosures revealed by the operation in the second case were helpful in formulating a clearer conception of the anatomic peculiarities of both patients. The end results of the two surgical procedures may be regarded as satisfactory, since the sterility was overcome in the first instance, and the dysmenorrhea completely relieved in the second.

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Discussion

DR. I. C. RUBIN.—In a fairly large experience with sterile women I have encountered various degrees of what I have called cervical phimosis, of which the second case of Dr. Dannreuther's is more particularly representative than the first case. In this condition there is a constriction of the vagina in front of the cervix, which varies from a diameter through which you can put your index finger to one which will admit only a lead pencil. The most extreme degree of vaginal phimosis is,

I believe, represented by Dr. Dannreuther's first case. I recently had a case which was the exact counterpart of his. This patient was also seen by Dr. Paul Titus of Pittsburgh who agreed as to the findings. The external os was just a tiny point in the center of a flat vaginal vault. By a sort of discussion operation a new vaginal portion of the cervix was formed. I dilated the cervical canal and packed petroleum jelly gauze into the denuded area representing the fornices and also inserted a gauze packing into the newly dilated cervical canal. A uterotubal insufflation done subsequently demonstrated tubal patency. The patient became pregnant six months later, went through a normal pregnancy and was given the test of labor. Unfortunately, the membranes ruptured prematurely. The cervix did not dilate satisfactorily so that after 36 hours, a cesarean section was done. Mother and baby did well.

In Dr. Dannreuther's case the patient was very fortunate because she became pregnant despite the fact that one tube was closed and the other open and lipiodol had been used.

These cases are not frequent, but they are not rare. The rarest type of cervical phimosis, I think, are the two varieties which Dr. Dannreuther has presented.

DR. DANNREUTHER (closing).—Perhaps cervical phimosis is a better term for the peculiar anomalies in these cases. It is comforting to know that Dr. Rubin was as dissatisfied with the end result in his attempted plastic procedure, as I was with mine in my first case.

VESICAL AND RECTAL INCONTINENCE IN THE SAME PATIENT*

Complete Laceration of the Perineum Following Childbirth and Large
Vesicovaginal Fistula Following Abdominal Panhysterectomy

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ON ADMISSION to the Carney Hospital on April 17, 1941, Mrs. L. J., a 49-year-old white woman complained of constant urinary incontinence. Three years before admission, she had had an abdominal panhysterectomy in a neighboring city, and this was immediately followed by urinary incontinence. Two months later, an operation was performed in an attempt to close a vesicovaginal fistula, but this was unsuccessful. In November, 1940, a second operation was attempted, with the same result, and in February, 1941, she was operated upon for the third time and still had constant urinary leakage through the vagina. The hysterectomy and the three operations for vesicovaginal fistula had all been performed in the same city. She was then referred to Dr. Roger C. Graves, Urologist-in-chief at the Carney Hospital for the transplantation of the ureters in the sigmoid. She had had no serious illnesses and no other operations. Menstruation was established at the age of 15, she had a 28- to 30-day cycle, the flow, which lasted from 3 to 4 days, was moderate in amount. She had had a surgical menopause three years previously. She had had five children who were all living and well, and no miscarriages. The only significant feature in her family history was that her mother had died of carcinoma of the stomach at the age of 75 years.

Examination

The physical examination revealed a woman small in stature, poorly developed and poorly nourished. The blood pressure was 120 systolic and 80 diastolic. The head and neck showed no gross abnormalities. The chest was symmetrical, the lungs were resonant and clear throughout and the heart, which was not enlarged, presented sounds of good quality; the rate was normal, the rhythm was regular, and there were no murmurs. The abdomen was thin and relaxed; the liver and spleen were not felt; there were no masses or areas of tenderness; there was a well-healed median pelvic incision. The vaginal examination revealed that the vulva, urethra and vulvovaginal glands were normal in development. The external genitals were excoriated, incrustated with urinary salts and the surface of the skin bled readily when touched with a gauze sponge. The perineum had been lacerated through the sphincter ani and the ends of the sphincter muscle were retracted laterally. There was no cystocele. The uterus had been completely removed with the adnexa. The vaginal vault showed marked scarring as the result of the four previous operations. At the summit of the vault there existed a vesicovaginal fistula which readily admitted the tip of the examining finger. A cystoscopic examination, performed by Dr. Graves, disclosed that the opening of the left ureter was in close proximity to the fistula while the opening of the right ureter was some distance away from it. After examination it was evident that if the ureters were transplanted

*Read at a meeting of the Obstetrical Society of Boston, January 18, 1944.

in the sigmoid that the urine would emerge from the rectum as it did from the vagina, since there was no anal sphincter to hold back the urinary flow. Two alternatives presented themselves: the first, closure of the vesicovaginal fistula through the vagina, the consultants believing that this could be accomplished; and the second, the reconstruction of the anal sphincter, the repair of the perineum, and, subsequently, the transplantation of the ureters in the sigmoid. The first course was decided upon and the patient was transferred to me.

Treatment

During the fourteen days which elapsed between April 17, and May 1, 1941, when the patient was operated on, she was kept in bed, the external genitals were irrigated with mild, warm acetic acid solution to dissolve the urinary salts incrustated on the skin, and the skin was covered by diachylon paste. At the end of April the parts were healed.

Operation on the Vesicovaginal Fistula

Under gas-oxygen, ether anesthesia, the external genitals and vagina were prepared with tincture of zephiran. A tight gauze pack was introduced in the vagina in an attempt to plug the hole in the bladder which was filled with sterile water. Dr. Graves passed a cystoscope and introduced a catheter in the left ureter in order to identify it while closing the fistula; the ureteral opening was found to be about 1 cm. away from the fistula. The fistula was in the vaginal vault, directed to the left and about 2 cm. in circumference. An incision was made in the scar tissue around the fistulous opening close to its edge, the vaginal wall was dissected away from the opening in all directions and it was possible to freely mobilize the bladder. The opening in the bladder was closed in a transverse direction with a running suture of No. 0 chromic catgut, using due care that the suture did not penetrate into the bladder. There was left a safe margin between the left end of the closed fistula and the catheter in the left ureter. This suture line in the bladder was reinforced by a series of No. 00 chromic catgut, interrupted sutures placed in the bladder muscularis. The bladder was tightly closed. The vagina was closed in a longitudinal direction in order to stagger the suture lines, using eleven interrupted sutures of No. 30 alloy wire, the ends of these sutures being arrested by lead shots. A plain No. 16 French, male soft rubber catheter, was introduced through the urethra and was attached to the right thigh. A small amount of bloody urine which had accumulated in the bladder was obtained. The patient was returned to bed in satisfactory condition. The ureteral catheter was left in and removed after 53 hours.

On May 17, 1941, since there had been no leaking of urine for 17 days, the patient was placed on an examining table in order to remove the metallic sutures. She was a very uncooperative, nervous, restless person. The first five sutures were removed without difficulty; while removing the sixth, she suddenly pulled up on the table so that the suture loop cut through the anterior vaginal wall. This was followed by the escape of a few drops of urine. She was put back to bed, constant drainage was re-established and I learned the lesson that these sutures should be removed under anesthesia. The small opening in the vaginal wall readily healed, and in a few days the catheter was removed and the patient was allowed out of bed, with a healed bladder. She had no difficulty in voiding from then on.

Operation for the Complete Laceration of the Perineum

On July 15, 1941, the patient was taken to the operating room; general anesthesia was administered, and the external genitals and vagina were prepared with tincture of zephiran. The remaining alloy wire sutures were readily removed; the bladder was well healed. The complete tear of the perineum was repaired, using the layer method. No. 0 and No. 00 chromic catgut were used throughout. One suture of prepared silk was passed through the skin and the united ends of the sphincter ani muscle to act as a splinting stitch. The primary result was entirely satisfactory.

Nine days after operation, the edges of the incision separated completely, there had been no infection, but the tissues had failed to heal.

The patient was again taken to the operating room on July 20, 1941, where general anesthesia was administered and the genitals were prepared as previously. The levator ani muscles were completely separated, the sphincter ends had separated despite the fact that the silk splinting stitch was still in place, but the vaginal part of the incision had completely healed. The edges of the separated incision were trimmed and curetted. The ends of the sphincter ani muscle were approximated by one interrupted suture of No. 2 forty-day chromic catgut. The edges of the levator ani muscles were approximated with a few interrupted sutures of the same material, and the rest of the perineum was closed with interrupted No. 30 alloy wire sutures, loosely tied. During her convalescence she was given large doses of vitamin C. At the end of two weeks the metallic sutures had been removed, the sphincter was healed, the perineum was healed except for a small area at the midpoint which was filling in rapidly, and she had good bowel control.

She was seen at the office on August 15, 1941, and a small granulating area at the middle of the perineum was discovered. On September 22, 1941, the perineum was almost completely healed, and gave good support. The sphincter was well healed. She was seen again on October 24, and November 7, 1941. On the last visit the following note was made: "The perineum is entirely healed and gives good support; the anus is well healed; she has satisfactory bowel control; The vesico-vaginal fistula is tightly closed." The findings on December 5, 1941, were the same as on November 7, 1941, and the patient was discharged cured.

Summary

A small, poorly developed, and poorly nourished, 49-year-old woman, the mother of five children, was referred to the Carney Hospital on April 17, 1941. She had had a complete laceration of the perineum at the birth of her first child. Three years before admission she had had an abdominal pahysterection and double salpingo-oophorectomy. The bladder was injured at operation with a resultant vesicovaginal fistula. Three operations had been done, without success, to close this vesico-vaginal fistula before her admission. The vesicovaginal fistula was closed through the vagina by means of alloy wire sutures. Subsequently the complete tear of the perineum was repaired. At the end of 9 days the perineal tissues had completely separated; no infection was present. The perineum was again sutured with alloy wire sutures. She was given large doses of vitamin C and the sphincter ani muscle and perineal body healed after the second operation. She was discharged with a healed bladder, voiding normally, with a healed sphincter ani and perineal body and with satisfactory bowel control.

ONE-DAY SULFONAMIDE TREATMENT OF CHRONIC GONORRHEA IN THE FEMALE

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THE revelation by Dees and Colston and by Reuter in May, 1937, that sulfanilamide is effective in the cure of gonorrhea, initiated many experiments in the sulfonamide treatment of this disease. The dosage schemes originally proposed were modified by others and the period of treatment abbreviated in various clinics. Marked variations in the reported results of this treatment could be ascribed to differences in the dosage, in duration of administration, and in the criteria of cure. The substitution first of sulfapyridine, then of sulfathiazole, sulfadiazine, and other compounds, has further complicated the picture. Sulfanilamide and sulfapyridine have now been displaced in the treatment of gonorrhea by the newer preparations because of their lessened toxicity and greater therapeutic effectiveness. With sulfathiazole and sulfadiazine too, there is variation in the recommended dosages and periods of administration. Some advise a ten-day course, while others have found five or seven days of treatment equally effective.

In previous reports on the treatment of gonorrhea in the female with sulfanilamide or sulfapyridine, we^{1, 2} noted that patients given either drug, whose treatment was stopped on the second to the fifth day because of some toxic reaction, were cured of gonorrhea in as high a proportion as those who continued with the medication for two weeks. Douglas³ has observed that gonococci disappear from the secretions within four to six hours after the beginning of sulfadiazine medication. At his suggestion, and at the suggestion of Mahoney and Van Slyke, we undertook to investigate the effect of the administration of sulfadiazine or of sulfathiazole during one day to a group of women all with cultures positive for the gonococcus.

The influence of war economy, taxing the nursing as well as the medical personnel and hospital administration, caused us to eagerly undertake this one-day treatment of gonorrhea. Prolonged medication may predispose to sensitization and by limiting the administration of the drug to one day, we hoped to avoid this possible sensitization.

Beginning in January, 1943, patients sent into our service at the Kingston Avenue Hospital with a culture report positive for the gonococcus, were given sulfonamide medication routinely for only one day.

A few patients, because of poor general condition, profound anemia, poor kidney function, or a history of intolerance to sulfonamides, were treated by other methods and are not included in this study. A complete history, physical and gynecological examination, complete blood count, and urine analysis, were first recorded. Patients were confined to the hospital but were ambulatory. They were on a general hospital diet. Fluids were forced before, during and after chemotherapy, the average intake was over 2,000 c.c. The day preceding the administration of the sulfonamide, each patient was given 32 grams of sodium bicarbonate.

The first group of patients (Group A) was given sulfadiazine 6 grams, during a single day—half at 9 A.M. and the other half at 3 P.M. An equal amount of sodium bicarbonate was administered at the same time.

TABLE I. GENERAL DATA ON ALL PATIENTS

	SULFADIAZINE		SULFATHIAZOLE
	GROUP A 6 GM.	GROUP B 8 GM.	GROUP C 8 GM.
No. Patients	96	97	88
Colored	59	61	54
White	37	36	34
Gonorrhea (alone)	76	83	66
Gonorrhea and syphilis	20	14	22
Age—Average	27 years	25.5 years	25.2 years
Oldest	44	47	49
Youngest	18	16	16
Weight—Average	133.3 pounds	127.3 pounds	131 pounds
Highest	300	187	338
Lowest	88	87	95
Colored (average)	132.1	124.2	132.0
White (average)	135.7	133.0	129.5

The second group (Group B) was treated identically except that 8 grams of sulfadiazine were administered during one day.

TABLE II. CLINICAL EXAMINATION BEFORE TREATMENT

	SULFADIAZINE		SULFATHIAZOLE
	GROUP A 6 GM.	GROUP B 8 GM.	GROUP C 8 GM.
Urethritis	46 patients	34 patients	30 patients
Skenitis	22	19	14
Bartholinitis	5	9	8
Cervical discharge			
scant	27	34	10
moderate	28	27	27
profuse	24	29	38
very profuse	17	7	5
Cervical erosions	36	27	21
Adnexal thickening	56	38	29
Adnexal masses	9	14	22
Adnexa negative	31	45	37

The third group (Group C) was given 8 grams of sulfathiazole in exactly the same fashion.

TABLE III. BACTERIOLOGIC FINDINGS ON ADMISSION
(REPORTED BY HEALTH DEPT.)

	SULFADIAZINE		SULFATHIAZOLE
	GROUP A 6 GM.	GROUP B 8 GM.	GROUP C 8 GM.
Culture +, smear +	13	15	26
Culture +, smear negative	80	71	58
Culture +, smear suspicious	3	11	4
	96	97	88

TABLE IV. NUMBER OF POSTTREATMENT CULTURES IN "CURED" CASES

	SULFADIAZINE		SULFATHIAZOLE
	GROUP A 6 GM.	GROUP B 8 GM.	GROUP C 8 GM.
Average number of cultures in all "cured" cases	5.4 culture	5.4 culture	4.1 culture
Average number of cultures in gonorrhea cases	5.1	5.3	4.1
Average number of cultures in gonorrhea and syphilis cases	6.5	5.7	4.1
Discharged after 2 cultures	1 patient	1 patient	0 patient
Discharged after 3 cultures	3	6	3
Discharged after 4 cultures	13	6	41
Discharged after 5 cultures	29	25	22
Discharged after 6 cultures	17	32	10
Discharged after 7 cultures	14	7	0
Discharged after 8 cultures	3	4	0
Discharged after 9 cultures	1	0	0
	81	81	76

TABLE V. FAILURES*—BACTERIOLOGIC FINDINGS

Sequential Appearance of Positive Culture or Smear	GROUP A			GROUP B			GROUP C		
	SULFADIAZINE 6 GM.			SULFADIAZINE 8 GM.			SULFATHIAZOLE 8 GM.		
	+	SUS. SMEAR ONLY	SUS. SMEAR NEG. CUL.	+	SUS. SMEAR ONLY	SUS. SMEAR NEG. CUL.	+	SUS. SMEAR ONLY	SUS. SMEAR NEG. CUL.
	NO. OF PATIENTS			NO. OF PATIENTS			NO. OF PATIENTS		
1st	3	1	2	5	0	0	3	0	0
2	2	0	1	3	0	1	3	1	2
3	1	1	1	3	1	0	0	0	1
4	1	0	0	0	1	0	0	0	1
5	0	0	1	0	0	2	0	1	0
6	0	0	1	0	0	0	0	0	0
No. of failures	—	—	—	—	—	—	—	—	—
Total No. of failures	15 patients			16 patients			12 patients		

*Including suspicious smears.

In all cases cultures and spreads were taken from the urethra and cervix (Skene's and Bartholin's, when indicated) the day following treatment and once or twice weekly during their hospital stay. The patients were examined gynecologically each week by the resident staff and also by the visiting staff working independently. The period of observation following chemotherapy averaged 30 days.

TABLE VI. FAILURES—DIVIDED INTO THREE GROUPS

	FAILURES						CULTURE NEGATIVE CULTURE POSITIVE CULTURE					
	TOTAL NUMBER TREATED	POSITIVE CULTURE NO.	POSITIVE CULTURE %	POSITIVE SMEAR NO.	POSITIVE SMEAR %	POSITIVE CULTURE OR SMEAR NO.	POSITIVE CULTURE OR SMEAR %	Negative smear no. No.	Negative smear no. No.	SUSPICIOUS SMEAR NO. No.	SUSPICIOUS SMEAR NO. No.	
Group A (6 Gm. sulfadiazine)	96	7	7.3	2	2.1	9	9.4	6	6.2	15	15.6	
Group B (8 Gm. sulfadiazine)	97	11	11.3	2	2.1	13	13.4	3	3.1	16	16.5	
Group C (8 Gm. sulfathiazole)	88	6	6.8	2	2.3	8	9.1	4	4.5	12	13.7	
Group A—Gonorrhea alone	76	7	9.2	2	2.6	9	11.8	5	6.6	14	18.4	
Group A—Gonorrhea plus syphilis	20	—	0	—	0	0	0	1	5.0	1	5.0	
Group B—Gonorrhea alone	83	11	13.3	2	2.3	13	15.6	2	2.4	15	18.0	
Group B—Gonorrhea plus syphilis	14	—	0	—	0	0	0	1	7.1	1	7.1	
Group C—Gonorrhea alone	66	4	6.1	2	3.0	6	9.1	1	1.5	7	10.6	
Group C—Gonorrhea plus syphilis	22	2	9.1	—	0	2	9.1	3	13.6	5	22.7	
Group A—Colored patients	59	3	5.1	—	0	3	5.1	2	3.4	5	8.5	
Group A—White patients	37	4	10.8	2	5.4	6	16.2	4	10.8	10	28.0	
Group B—Colored patients	61	2	3.3	—	0	2	3.3	2	3.3	4	6.5	
Group B—White patients	36	9	25.0	2	5.6	11	30.6	1	2.8	12	33.4	
Group C—Colored patients	54	1	1.9	1	1.8	2	3.7	4	7.4	6	11.1	
Group C—White patients	34	5	14.7	1	2.9	6	17.6	—	0	6	17.6	

Results

In Table VI we see that the failures proved by positive smear or culture were 9.4 per cent in Group A, 13.4 per cent in Group B and 9.1 per cent in Group C. There is no appreciable difference in effectiveness between sulfadiazine and sulfathiazole as used in this study. In each of the groups the percentage of patients with persistently positive smears and cultures was much larger among the white than among the colored patients (Group A—5.1 per cent colored vs. 16.2 per cent white); [Group B—3.3 per cent colored vs. 30.6 per cent white]; (Group C—3.7 per cent colored vs. 17.6 per cent white).

It had previously been observed that patients under treatment for both syphilis and gonorrhea had fewer failures than those with gonorrhea alone. In Table VI we find this difference very striking. In Groups A and B there were no failures among the syphilis plus gonorrhea cases, whereas in the gonorrhreal cases of Group A failures were 11.8 per cent and in Group B 15.6 per cent. In Group C, however, there was no such difference.

From Table VII we find that the percentage of failures by smear and culture of all colored patients in the three groups combined was 4.1 per cent whereas the whites failed in 20.9 per cent. Colored patients of all three groups treated for gonorrhea alone failed in 5.8 per cent, while whites failed in 21.0 per cent.

TABLE VII. FAILURES, THREE GROUPS COMBINED, RACIAL DIFFERENCES

	NUMBER TREATED	FAILURES				POSITIVE CULTURE OR SMEAR, OR SUSPICIOUS	
		POSITIVE CULTURE ALONE		POSITIVE CULTURE OR SMEAR		NUM- BER	%
		NUM- BER	%	NUM- BER	%		
Colored patients	171	6	3.5	7	4.1	15	8.8
White patients	110	18	16.39	23	20.9	28	25.5
Gonorrhea alone, all races	225	22	9.8	28	12.0	36	16.0
Gonorrhea plus syphilis, all races	56	2	3.6	2	3.6	7	12.5
Gonorrhea alone, colored	125	6	4.8	7	5.8	11	8.8
Gonorrhea alone, white	100	16	16.0	21	21.0	25	25.0
Gonorrhea plus syphilis, colored	46	0	0.0	0	0.0	4	8.7
Gonorrhea plus syphilis, white	10	2	20.0	2	20.0	3	30.0

Considering the white patients, those treated for gonorrhea alone failed in 21.0 per cent while those treated for syphilis and gonorrhea failed in 20 per cent. Among the 46 colored patients treated for both gonorrhea and syphilis there was not a single positive smear or culture after treatment, whereas among the colored treated for gonorrhea only 5.1 per cent had a positive smear or culture after treatment. There is therefore not only a considerable difference in failures between the races, but there seems to be in the colored race an improvement of the results as a consequence of the coincidental antisyphilitic treatment.

In Table VIII it is seen that in Groups A and B (sulfadiazine cases) the failures weighed an average of 15.5 and 13.7 pounds more respectively than the average of their group. In Group C there was no significant difference in weight.

TABLE VIII. AGE AND WEIGHT OF FAILURES COMPARED WITH ALL CASES TREATED

	GROUP A	GROUP B	GROUP C
Average age of failures	27.1 years	25 years	23.7 years
Average age, all cases	27.0	25.5	25.2
Average weight of failures	148.8 pounds	141.0 pounds	128.0 pounds
Average weight of all cases	133.3	127.3	131.0
Average weight of white failures	160.6	142.7	130.8
Average weight of white, all cases	135.7	133.0	129.5
Average weight of colored failures	134.5	137.8	124.1
Average weight of colored, all cases	132.1	124.2	132.0

In none of the three groups was age a factor.

In Table IX the cure rates in the three groups are listed. The cases with suspicious smear reports and negative cultures constitute a doubtful category, which we have listed as failures in the upper part of the Table, for the sake of conservatism in the interpretation of results. For practical purposes and for comparison with other reported series, this group with suspicious smears is ignored and results are based only upon positive smear or culture reports.

TABLE IX. ANALYSIS OF CURES, DIVIDED INTO THREE GROUPS

	SULFADIAZINE			SULFATHIAZOLE		
	GROUP A		GROUP B		GROUP C	
	6 GM.	8 GM.	8 GM.	8 GM.	8 GM.	8 GM.
Total number patients treated	96		97		88	
Including suspicious smears						
Failures	15	15.6	16	16.5	12	13.6
Cures	81	84.4	81	83.5	76	86.4
Excluding suspicious smears						
Failures (positive smear or culture)	9	9.4	13	13.4	8	9.1
Cures	87	90.6	84	86.6	80	90.9

Major toxic symptoms were not observed in this series of cases. The average concentration of sulfadiazine in blood taken three hours after the last dose in 36 patients of Group A was 4.2 mg. per cent, while it averaged 6.0 mg. per cent in 72 patients in Group B.

Most of the failures following the one-day treatment had a week of rest, then were given four grams of sulfathiazole daily for seven days. We⁴ had previously found that sulfathiazole four grams daily for seven days gave us a 95.0 per cent cure rate. This sulfathiazole course rendered most of them bacteriologically negative.

Summary

Three groups of hospitalized women with chronic gonorrhea, proved in every case by a positive culture, were treated by means of sulfadiazine or sulfathiazole administered during one day. Methods of follow-up and technique of bacteriologic examination were unchanged.

The percentage of bacteriologic failures differed little in the three groups. Major toxic manifestations were absent. Age of the failures did not differ significantly from the average in each group. With sulfadiazine the average weight of the failures was 14 to 15 pounds greater than the average weight of all the patients treated with this drug. With sulfathiazole there was little difference in weight between the failures and the entire sulfathiazole group.

There was a definite racial difference in results, the failures in the white patients being three to four times greater than in the colored. This observation had previously and independently been made by others.^{5, 6} In the colored the coincidental treatment of syphilis seems to improve the results of the treatment of gonorrhea. We do not know whether the better therapeutic results of the colored patients treated for gonorrhea with sulfonamides is due to a superior racial immunologic response, or to better reaction to the sulfonamides due to the pigmentation of the skin.

Conclusions

The administration of sulfadiazine or sulfathiazole during a single day to hospitalized women with cultures positive for the gonococcus was followed by the disappearance of gonococci in 86.6 per cent to 90.9 per cent of the cases. There was no significant difference of results following 8 Gm. sulfathiazole, 8 Gm. sulfadiazine or 6 Gm. sulfadiazine. There was a difference in response of patients of the colored and white races, the failures being three to four times greater in the whites.

We are not ready to advocate the general use of the "one-day treatment" of gonorrhea and believe that it should be used only in hospitalized patients when time is at a premium.

The laboratory part of this study was conducted under the supervision of Dr. Philip Rosenblatt to whom we hereby express our thanks.

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TORSION OF OVARIAN CYSTS IN CHILDREN

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THE rarity of ovarian cysts with torsion of the pedicle in children justifies the report of the following two cases which occurred recently. Through 1925 a total of 99 cases of ovarian cysts in children had been reported in the American and English literature,¹ over 50 per cent of these being in children approaching puberty.² Out of 12,260 admissions to the Boston Children's Hospital in 1929, there was reported by Lanman only one torsion of an ovarian cyst and this in an older child.³ Since the opening of the Fayetteville City Hospital in 1912, there has been only one case of torsion of an ovarian cyst in a child under five years of age, and, since July 1, 1930, only one case of an ovarian cyst with a twisted pedicle in a child of twelve years. There was one twelve-year-old girl with hydrosalpinx and a small cystic right ovary with torsion of the tube, and a fourteen-year-old child with a ruptured right ovarian cyst without torsion.

CASE 1.—The following case occurred in a four-year-old white female child. The child had been perfectly well. On July 30, 1943, she ate her usual breakfast about 7:30 A.M. Shortly afterwards she went to stool and immediately cried out in pain. She vomited her breakfast and nausea followed. The nausea and vomiting continued throughout the day and night. The child ate nothing and lay quietly except when seized with pain, when she would lie on her abdomen, draw up her knees, and moan in what appeared to be paroxysms of abdominal pain.

The child had an attack of tonsillitis two weeks previously from which she quickly recovered without known ill effects. She was born February 10, 1939, the labor being a normal one of five hours' duration. She had been immunized for diphtheria at six months, pertussis at eight months, smallpox at nine months, one and one-half and two years, and typhoid at two years. She was said to have had occasional colds and attacks of tonsillitis in the past. Internal strabismus of the right eye was first noticed in February, 1942. Development was otherwise normal.

The family history was significant in that both the mother and maternal grandmother had ovarian cysts removed surgically.

On admission to the hospital, July 31, 1943, on the second day of illness, the symptoms continued unabated. The pain was not definitely localized, but seemed more intense around the umbilicus, and tenderness was chiefly on the right side at McBurney's point. The patient's blood count was as follows: red blood cells, 4,330,000, hemoglobin 70 per cent, leucocytes 10,480, eosinophiles 1, stabs 1, segmented 74, lymphocytes 23, and monocyte 1. Two later blood counts were made the same day, with little variation. The urinalysis showed: reaction 6.0, acid, specific gravity 1.040, albumin negative, sugar negative, occasional red blood cell, and occasional white blood cell. The following morning the child took some nourishment and seemed to be in better condition. The total leucocyte count was 11,900, with stabs 2, seg-

mented 83, and lymphocytes 15. Urinalysis showed: reaction 6.0, specific gravity 1.020, albumin faint trace, pus 3 to 5 per high power field, and no red blood cells. There were several paroxysms of severe abdominal pain during the day. A single bowel movement was loose, and no blood was present. The most commonly reported symptoms of torsion of ovarian cysts, frequency and dysuria, were not present. Rectal examination showed a movable mass in the midline about the size of a man's thumb. At noon the leucocyte count was 18,900, stabs 4, segmented 77, and lymphocytes 17. About midafternoon the leucocyte count was 13,900, stabs 4, segmented 66, lymphocytes 29, and monocyte 1. The differential diagnosis at this time was: (1) intussusception, (2) acute appendicitis, (3) pyelitis, (4) ovarian cyst. Three consultants saw the patient during the day. Surgery was not advised even though a mass could be felt and the differential count was elevated.

The child's pain continued during the night and she appeared more ill. Operation was performed on August 2. A lower midline abdominal incision was made, and abundant serosanguineous fluid was found in the peritoneal cavity. The right ovary and tube immediately presented in the wound, and were twisted on their pedicle three times. Both appeared gangrenous. The ovary was cystic, about five centimeters in diameter, and the tube enlarged in diameter about four times. Both were removed by ligating the pedicle and excising the tube and ovary. The raw surfaces were peritonealized with continuous Dulox suture. The left tube, and ovary and the uterus were normal. The appendix, which was bound down by adhesions and subacutely inflamed, was also removed, the stump being treated with carbolic acid and alcohol and inverted by means of a purse-string suture. The blood vessels on the right side appeared gangrenous up to the iliac crest. Closure was made without drainage.

The child made an uneventful recovery except for a small cutaneous abscess at the upper angle of the wound.

The following points are of interest in this case: Torsion probably occurred after defecation. There was no rigidity, no temperature, and the patient was not acutely ill. Following the acute onset, the patient took normal nourishment and had normal defecation. There was no abdominal distention. The pain occurred in paroxysms. A mass was present rectally in the midline.

While the preceding report was typical of an acute torsion, the following case was more subacute, or chronic in nature.

CASE 2.—This patient was first seen on April 1, 1942. She was a twelve-year-old girl whose chief presenting symptom was pain occurring in paroxysms in the lower left side of the abdomen. She was nauseated and vomited. The child's mother was a nurse and requested that she remain at home. She was admitted to the hospital the following day. Throughout the night the pain continued in paroxysms, some of which lasted as long as thirty-five minutes. The leucocyte count was 11,000, with eosinophiles 3, stabs 1, segmented 47, and lymphocytes 49. The urinalysis was negative. There was a fullness in the lower left quadrant with tenderness, but no rigidity. There had been no other illness of consequence, but for a year and a half previously, the child had complained of severe pain in the lower left side upon exertion. For the past six months there had been a thick dark vaginal discharge about every four weeks and at this time the pain was accentuated. The family history was irrelevant.

The patient stayed in the hospital four days and during this time the symptoms abated. She was discharged on April 7. About 5 A.M., April 9, the pain became much worse, and was associated with nausea. The leucocyte count at this time was not elevated. A mass about which there had been some doubt previously was now plainly felt in the lower left quadrant. The following day the mass seemed larger. The leucocyte count was elevated to 15,850, with segmented 76, and lymphocytes 24. Later the leucocyte count was 14,350 with 84 polymorphonuclears and 16 lymphocytes. The diagnosis was undetermined, but operation was advised. A midline incision was made, and bloody fluid was present in the abdominal cavity. A mass consisting of the left tube and ovary filled the greater part of the pelvis. The tube and ovary had been twisted several times, and the tube was gangrenous. The ovary was enlarged to about seven and one-half centimeters in diameter. A portion of the cyst, containing blood, was ruptured in untwisting the pedicle to liberate the mass. The left tube and ovary were clamped and excised. The stump was sutured with continuous 20-day number 2 catgut, and the raw surfaces were peritonealized. The appendix was normal, but was removed with inversion of the stump. Other organs were normal. Closure was in layers without drainage. The ovary consisted of a small cystic portion containing dark blood, and a solid portion which was a dermoid cyst containing four well-formed teeth.

The patient made an uneventful recovery.

The cyst had probably been present for about a year and a half prior to its recognition. Partial torsion must have occurred with the onset of the first severe attack of pain. The pedicle did not remain twisted, nor did the true cause of pain become manifest until the mass enlarged, due to hemorrhage occurring in the cyst when the venous return was cut off and the arteries were still pumping blood.

Discussion

These two cases of ovarian cyst with torsion of pedicle were reported because of their rarity and the interesting points in their diagnosis. The diagnosis was obscure in the beginning, being confused with intussception, acute appendicitis, and pyelitis. Neither case presented what are commonly considered characteristic symptoms, frequency and urgency. The presence of a pelvic mass palpated rectally should be almost conclusive evidence of a cyst. The condition in children would be recognized more frequently prior to operation if the possibility of torsion of an ovarian cyst were considered. The treatment is always surgical. The prognosis is good in children if operation is performed before peritonitis sets in.

Summary

In summary, two cases of torsion of an ovarian cyst, one acute, the other chronic, are reported. One was an acute torsion of a simple cyst on the right side in a four-year-old child, while the other was a subacute, or chronic, torsion of a dermoid cyst on the left side in a twelve-year-old child. Both were accompanied by torsion of the tube and hemorrhage into the cyst. Frequency and dysuria were not a factor in either case. Symptoms followed defecation in one case, while no known precipitating factor was found in the other. The pain occurred

in paroxysms in both. There was no rigidity or temperature, and the patients were not acutely ill, even though operation was delayed in both cases. A pelvic mass was palpated rectally in one patient, abdominally in the other.

Conclusion

Twisted ovarian cysts should be considered in any differential diagnosis of lower abdominal pain in female children.

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26 NORTH COLLEGE AVENUE

PELVIC ACTINOMYCOSIS TREATED BY SURGERY AND ROENTGEN RAY, WITH RECOVERY

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ACTINOMYCOTIC infection of the internal genitalia of the female is uncommon and recovery is rare. Eighty-five cases of actinomycosis of the female pelvic organs have thus far been reported, of whom only 7 have survived. We wish to report an additional case apparently cured of this malignant disease.

Cornell in 1934 published a comprehensive survey of previously reported cases, of which there were seventy-one, to which he added one of his own. Thirteen cases have since been reported, four by Cote and Tudhope, two by Counseller and Horner and one each by Rumpf, Gardiner and Welsh, Morris, Joseph and Sommeral, Masson, Schocksert and de Cooman, Junghaus and Hüssy, bringing the total to eighty-five.

Gardiner and Welsh reported that only four cases had apparently recovered, namely, those of Horalek, Müller, Martius, and Schugt, all of whom had been treated by surgery and x-ray. A patient of Cornell's, who was operated upon and later treated with potassium iodide, was well four years after operation. Masson reported a case apparently cured by operation and x-ray. A patient of Sanford's was in good health three years after treatment with potassium iodide, roentgen ray and radium. Of the seven cured cases, therefore, five were treated by surgery and x-ray, one by surgery and potassium iodide, and one by surgery, potassium iodide, x-ray and radium.

Case Report

Mrs. E. P., a white woman 30 years of age, was admitted to the New York City Hospital on May 25, 1934. She complained of pain in the right lower abdomen, sacral backache, chills, fever, and retention of urine. Her past history included an attack of diphtheria in 1927, and extraction of carious teeth in September, 1933. Menstruation was normal. She had had two normal deliveries, the last in 1931.

Her present illness began in January, 1934, with an attack of sharp pain in the lower abdomen, followed by chills and fever, lasting a week. These symptoms subsided, but three similar attacks followed, during the four months before admission to the hospital. With the last attack she began to have difficulty in urination.

Physical examination revealed an emaciated, anemic, feverish young woman. Teeth and gums were in poor condition. The abdomen was tense, distended, and extremely tender over its lower half. There was moderate rebound tenderness and slight rigidity in the right lower quadrant. A mass could be outlined in the lower abdomen, extending almost to the umbilicus. The cervix was displaced forward against the symphysis by a bulging mass in the cul-de-sac. The uterus was not separately made out.

The temperature curve was of the septic type. The leucocyte count was 16,900, with 82 per cent polymorphonuclear leucocytes. There was a moderate secondary anemia, and a rapid sedimentation rate. Urine showed a trace of albumin and a few casts. X-ray of the chest and blood Wassermann were negative.

A preliminary diagnosis was made of acute exacerbation of chronic pelvic inflammatory disease, with pelvic abscess.

On May 28, the pelvic abscess was drained by posterior colpotomy. A quart of foul-smelling, greenish pus was obtained. The laboratory examination did not show sulfur granules or actinomycetes. Following the colpotomy, the patient's condition improved only temporarily. During the next seven months, three more colpotomies were performed, pus being evacuated each time. In spite of these repeated drainages of the cul-de-sac, the patient continued to be seriously ill, with a high septic temperature, rapid sedimentation rate, hyperleucocytosis, and severe secondary anemia. Repeated blood transfusions were given.

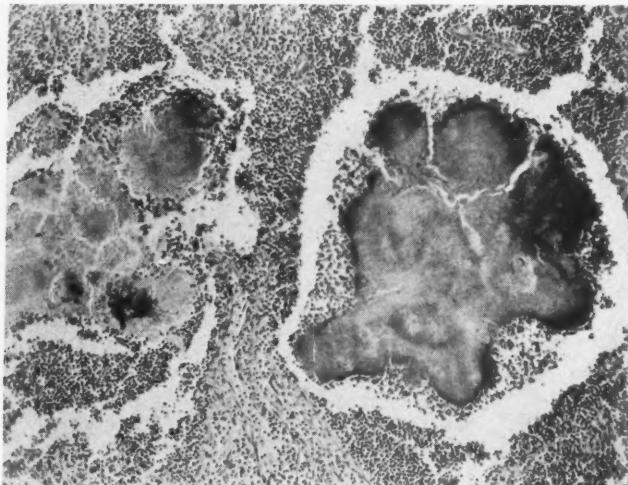


Fig. 1.—Lobulated masses of mycelium in the liquid pus of an actinomycotic abscess.

When the temperature had remained normal for a month, although the sedimentation rate was still rapid, laparotomy was performed on December 10, 1934. There was a dense network of easily separated adhesions in the pelvis, with tubes, ovaries and uterus agglutinated to the cecum, sigmoid, rectum and anterior abdominal wall. The process grossly resembled that seen in cases of acute gonorrhreal adnexitis following repeated recurrences. The tubes were dilated, thick-walled, tortuous, and contained thick pus. A bilateral salpingo-oophorectomy and supracervical hysterectomy was done. The pelvis was then drained through the posterior colpotomy wound and through the lower angle of the abdominal incision.

Pathology.—The pathology of this case was reviewed in detail by Lisa and Levine in the *Archives of Pathology*, January, 1937, and will be given here but briefly.

Gross Findings.—The specimen consisted of a uterus with an adnexal mass, and a separate tuboovarian tumor. The supracervically ampu-

tated uterus was grossly and histologically normal. The distal half of the attached tube was incorporated in a mass $4\frac{1}{2}$ cm. in diameter, covered by a thick grayish-yellow exudate. On section, the tube and ovary could not be differentiated with certainty. The proximal half of the tube was free and very broad. It was covered with a thick granular serosa. On section, the wall was dense and firm. The lumen was dilated by a light-gray gelatinous material, surrounded by a narrow yellow zone. The separate tuboovarian mass was much larger, measuring 7 by 5 by 4 cm. It was similar to the attached mass, except that no free tube was present.

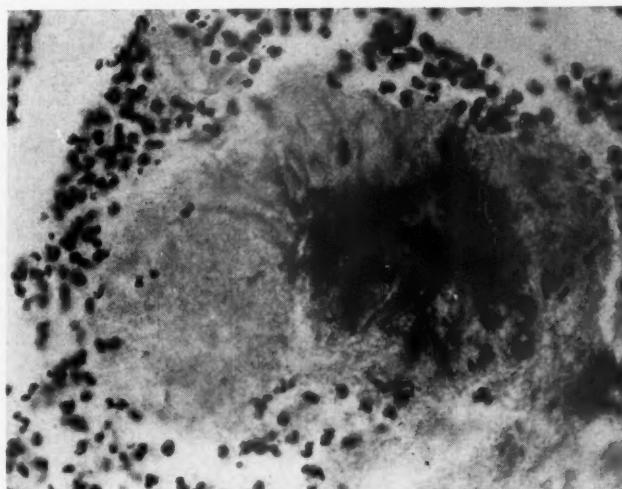


Fig. 2.—Filamentous structure of the central tangle of a knot of mycelium.

Microscopic Findings.—The adnexal tumors consisted of multiple actinomycotic abscesses containing lobulated masses of mycelium in liquid pus (see Fig. 1). The borders of the mycelium knots showed distinct radiation. Formation of typical clubs could be observed. On higher magnification the central tangles of the knots revealed a typical filamentous structure (Fig. 2). The immediate vicinity of the abscesses was converted into granulation tissue with some scar formation, indicating the chronic character of the actinomycotic granuloma (see Fig. 3). The granulation tissue consisted chiefly of mononuclear cells. The borders of the abscesses were necrotic, with abundant leucocytic infiltration.

A moderately severe wound infection developed four days after operation. Cultures showed streptococci and various bacilli. The infection responded to the use of Dakin's solution and the ultraviolet ray. In addition to blood transfusions and iron ammonium citrate, maximal doses of potassium iodide were administered. The patient was discharged much improved on January 15, 1935. At this time she weighed 102 pounds. Her weight had been as low as 72 pounds while in the hospital.

Several weeks later she appeared at the follow-up clinic with a tender, indurated mass measuring 7 to 8 cm., in the left lower quadrant of the abdomen. After another three weeks the mass had increased to

10 cm. in diameter, and a second mass had appeared on the right side, hard, fixed, and adherent to the anterior abdominal wall. Since potassium iodide had been ineffective in prevention of recurrence, its use was discontinued, and the patient was referred to the x-ray department of the Woman's Hospital, for x-ray therapy.

Roentgen Ray Treatment.—Treatment was begun tentatively, as there was not (and is not now) any established dosage procedure for abdominal actinomycosis. The tender, indurated mass in the left lower quadrant, measuring about 10 cm. in diameter, was first attacked. It was treated daily, starting February 25, 1935, through alternate anterior and posterior portals, at the rate of 300 roentgens per day.

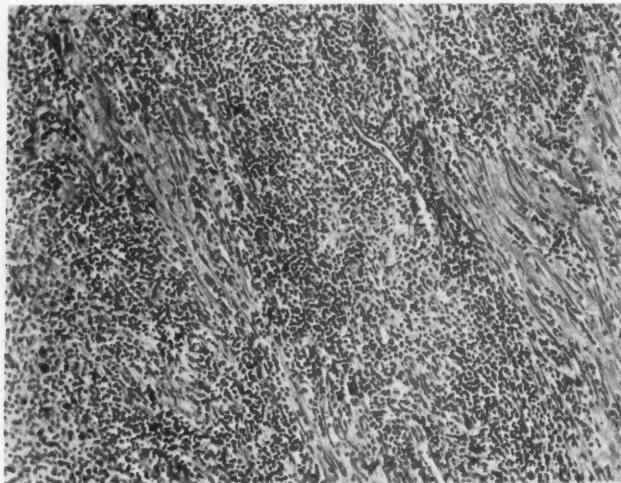


Fig. 3.—Tissue of actinomycotic granuloma (scar formation).

Other factors were 200 kilovolts peak, 30 milliamperes, 70 cm. target-skin distance, 0.5 mm. to 1 mm. copper filter. Total roentgens in first cycle, 2,100 anterior, 2,100 posterior, given in a period of 3 weeks. The mass gradually diminished in size. A small residue was again treated in June, 1935, giving 100 r. daily to alternate anterior and posterior fields up to a total of 1,000 r. each. Two months later, in August, 1935, it had completely disappeared.

The right-sided mass, located at a higher level in the abdomen than the left and firmly attached to the anterior abdominal wall, was more recalcitrant. Treatment on it was commenced March 20, 1935, and continued at intervals until September 18, 1935. The first cycle, given more slowly than the first cycle on the opposite side, accumulated a total of 2,400 r. to each of the two portals used, over a period of seven weeks, ending May 9, 1935. On May 24, the mass seemed larger, and as the skin was in good condition, another cycle, totaling 1,800 r. anterior and 1,800 r. posterior was given. The mass shrank, but did not disappear, and from August 30 to September 18, 1935, a third and last cycle totaling 1,500 r. anterior and 1,500 r. posterior was given. Skin reactions were never excessive. The skin was in good condition at the end of the treatment, and remained so. By the end of November, 1935, there was no evidence of disease, and it has not recurred to date.

The patient received over her left-sided lesion totals within four months, of 3,100 r. (in air) to each of two opposing fields, anterior and posterior. The right-sided lesion, over a period of six months, received 5,700 r. per field, 11,400 r. altogether. The latter is among the highest doses reported in the cure of abdominal actinomycosis. The patient showed little evidence of satisfactory regression before the last cycle was given, so it seems unlikely that she was overtreated.

Follow-Up.—The patient was examined in March, 1940. She felt very well. There were no abdominal symptoms. Her bowels moved regularly. There was no pain, vaginal discharge or urinary symptoms. The cervix was freely movable, the parametria shortened, but contained no masses. Her weight was 149 pounds, a gain of 77 pounds since her lowest point in 1934.

She was seen again on February 17, 1944. She had no complaints. Her bowels moved regularly. The abdominal panniculus is moderate. There is a well-healed lower left paramedian cicatrix, with an umbilicated retraction at the lower angle, and a left lateral transverse scar about the middle of the incision, extending out for a distance of 1½ inches. Pelvic examination reveals the stump of a freely movable cervix. No adnexal or parametrial masses can be felt. Her weight is 148 pounds. There is a gain of 76 pounds since her lowest point in 1934.

Although first seen ten years previously, the purpose of this belated report is to note the complete recovery of the patient after this lapse of time.

Summary

The clinical picture presented by our patient before operation was one of protracted, severe pelvic suppuration, with septic temperature, severe secondary anemia, and emaciation. Posterior colpotomy was performed on four occasions for the drainage of pus collections in the pelvis, with only temporary benefit.

Laparotomy was performed six and a half months after admission to the hospital, although the blood sedimentation rate was still very rapid. At operation, the findings resembled those commonly seen in cases of recurrent pelvic suppuration with tuboovarian abscesses.

In spite of hysterectomy and bilateral salpingo-oophorectomy, followed by large doses of potassium iodide, there was prompt recurrence in the abdomen. Roentgen ray treatment resulted in disappearance of the recurrences. The method employed, namely, surgery followed by fractional x-ray treatment with high total dosage, is probably the most effective in the treatment of abdominal actinomycosis.

Follow-up examination, five and ten years later, disclosed that the patient was well and there was no evidence of abdominal or pelvic disease.

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Special Article

OPHTHALMIA NEONATORUM*

With Special Reference to the Sulfonamides in Treatment and the Continued Importance of Silver Preparations in Prevention

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IN THE school year 1906 to 1907, 28.2 per cent of the pupils admitted to schools and classes for the blind were blind because of ophthalmia neonatorum. In the school year 1941 to 1942, the percentage was 5.6.† These figures emphasize the great importance of the use of silver nitrate in the prevention of ophthalmia neonatorum and the value of the campaign waged by the National Society for the Prevention of Blindness for the use of this preventive measure.

The present communication is concerned chiefly with the newer methods of treatment, especially the use of the sulfonamides.

Recent studies seem to indicate^{1, 2} that silver is still the best preventive measure. However, silver nitrate also has its limitations in prevention. This has been demonstrated by Lehrfeld's³ study of approximately 28,000 hospital birth records and 2,000 cases of ophthalmia neonatorum.

That silver acetate should be given consideration instead of silver nitrate is suggested by the studies of Rambo.⁴ He found that in Hungary, a one per cent solution of silver acetate is used as a prophylactic for ophthalmia neonatorum. The advantage of this salt over silver nitrate is its safety. A one per cent solution of either salt is equally effective in preventing gonorrhreal ophthalmia. The solubility of silver nitrate is very high, one gram being soluble in 0.4 gram of water. The solubility of silver acetate solution is one gram to 100 c.c. of water. Because of the low solubility of silver acetate, a stronger solution than is needed for infants' eyes cannot be prepared with water at room temperature. Rambo believes that "silver acetate has other properties, however, which would appear to make it more suitable to the needs of practice than the nitrate. While the latter is readily soluble in water, its solutions may gradually become concentrated by evaporation. Silver acetate crystallizes out as soon as a concentration of 1.2:100 is reached. Thus the danger of using too concentrated a solution is entirely precluded in the case of silver acetate."

*Aided by a grant from the Ophthalmological Foundation, Inc.

†Percentage of blind children in the United States.

That silver proteins should not be used as substitutes is proved by the work of Muir⁵ and Menshutin.²

The use of sulfonamides in the treatment of ophthalmia neonatorum has been discussed recently by numerous observers. Among these are Jensen⁶ in 1939, Herman⁷ in 1940, Schreiner,⁸ Blanton⁹ and Kadlicky¹⁰ in 1941, and Demicheri, Chiazzaro and Uriarte¹¹ in 1942.

Gonorrhreal ophthalmoblenorrhea has been successfully combated with sulfapyridine by Thrane.¹² Sourdille¹³ reported a case of gonococcic ophthalmia successfully treated with di-(p-acetylaminophenyl)-sulfone. McKee¹⁴ described the case of a man with the typical appearance of severe gonorrhreal ophthalmia. Fifteen grains of sulfanilamide with 5 grains of sodium bicarbonate every six hours internally as well as the usual local treatment were administered. The discharge was noticeably less on the third day and had almost disappeared by the fifth day.

Blumberg and Gleich¹⁵ believe that the sulfonamides used in the treatment of gonococcic ophthalmia neonatorum have greatly decreased the duration of the disease and have practically eliminated complications. Patients in their hospital are now treated routinely only with the oral administration of sulfathiazole. Local therapy and mechanical protection of the unaffected eye are apparently unnecessary. Sulfathiazole in doses of 1 grain per pound of body weight cured their patients and prevented complications.

The successful administration of the sulfonamides in the treatment of gonococcic conjunctivitis has been reported by Lewis¹⁶ in 120 patients. Toxic reactions, with the exception of one case, early in the series, were practically negligible. Nausea occurred frequently, especially with the administration of sulfapyridine. Slight cyanosis was rather common. In very few cases were there any significant changes in the blood cell counts or in the hemoglobin. According to Lewis, there seems to be no contraindication to the systemic use of the sulfonamides except a definite history of previous intolerance to the drugs. He found the following: "Sulfapyridine is amazingly effective in the treatment of gonococcic infections of the eye. Sulfathiazole is apparently somewhat less effective. Both are definitely superior to sulfanilamide. A cure may be expected within three days, as a rule, from the time sulfapyridine treatment is begun." Recently, Lewis tried a 5 per cent solution of sodium sulfathiazole, instilled locally every two hours, combined with the usual dose of sulfathiazole internally. Apparently it is of definite value. He believes every patient with gonococcic conjunctivitis should immediately be given adequate systemic treatment with sulfapyridine or sulfathiazole.

According to Barbour and Towsley¹⁷ sulfanilamide is a definite advance in the therapy of ophthalmia neonatorum for the following reasons: (1) The incidence of corneal complications has been diminished.

(2) Hospitalization has been reduced to an average of eight days with a minimum of complications but newborn infants tolerate and require larger quantities of the drug than adults to raise the blood concentration to the expected level.

In Muir's opinion⁵ while sulfanilamide has produced more brilliant results than any previous therapeutic measure in the treatment of gonorrhreal ophthalmia, it must be used with caution and a full understanding of its potential dangers. Muir believes that there will continue to be cases of gonorrhreal conjunctivitis resistant to sulfanilamide, for which recourse to all available therapeutic resources will be necessary to prevent loss of the eye.

For the sulfonamide-resistant group, penicillin seems to offer great hope in general gonorrhreal infections resistant to the sulfonamides. From several cases which have come to my attention, the same condition seems to be true concerning the local or general use of penicillin in eye infections caused by the gonococcus. If neither the sulfonamides nor penicillin prove effective, artificial fever therapy should be considered.⁵ Mercurochrome¹⁸ and other drugs have received consideration both in prophylaxis and treatment but greatest reliance should still be placed on silver nitrate and the sulfonamides (especially sulmyd [sulfacetamide]).^{19, 20}

Once ophthalmia neonatorum has developed even the best treatment available often leaves many blind children, which are a burden either to the state or to the parents. It is important for physicians, especially obstetricians and ophthalmologists, to give serious consideration not only to the treatment but also to the prevention of ophthalmia neonatorum.

Safeguards for the prevention and treatment of ophthalmia neonatorum must be set up, that is: (1) Prenatal prevention—diagnosis and treatment of infections in the prospective mother; (2) Postnatal prevention—the use of a prophylactic in the eyes of the newborn infant and (3) universal use of the most modern and effective methods of treatment.

Because our knowledge of improved treatment of ophthalmia neonatorum apparently has lessened the hazards of this disease, it does not mean that preventive measures and prophylactic procedures should be discarded. Prevention is always preferable to cure regardless of the success of the treatment. In addition newborn infants are frequently attended by midwives or physicians at home deliveries in isolated communities and it could not be assumed that the necessary treatment facilities would be readily available.

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35 EAST SEVENTIETH STREET

Department of Book Reviews

CONDUCTED BY ROBERT T. FRANK, M.D., NEW YORK

Review of New Books

Endocrinology: Gynecology and Obstetrics

Female Endocrinology Including Sections on the Male¹ is a sincere and earnest attempt to present the rapidly accumulating evidence covering this interesting field. The author has worked for many years, both in the laboratory and in the clinic, which, together with his wide knowledge of the literature, enables him to give a full presentation.

The volume is divided into three sections—physiology, clinic and laboratory. Of this, physiology covers 286 pages, which include development, the function of the ovary from every aspect. The safe period, the endocrine factors in menstruation and uterine motility are discussed. The endocrine role of the placenta, the physiology of parturition are taken up as well as that of the breasts. A chapter is devoted to the physiology of the testis. After this, the function of all individual endocrine glands is dealt with, with particular regard to any connection with the genital sphere. These chapters are very satisfactory, being complete, yet short and incisive and complimented, as is carried out through the book, by a satisfactory bibliography.

The clinical portion covers particularly the functional diseases, including deficiencies and excesses of menstruation. Here the innumerable etiological causes assigned by various authors are discussed in the light of the large experience of the writer. It is not surprising that in this very debatable field the reviewer is unable to agree with many of the interpretations. However, in the main, the therapeutic measures recommended are conservative and justifiable. The same applies to even a greater degree to the chapter on dysmenorrhea and spontaneous and habitual abortion. In the latter, the Rh factor has not as yet been incorporated. A chapter on abnormal manifestations arising during gestation, covers toxemias, endocrine aspects of dystocias and maternal tetany. Abnormalities of the breast are taken up. An excellent chapter on obesity follows. Preceding the discussion of the long list of endocrinopathies, is a chapter on constitutional types. The clinical portion of the book ends up with the discussion of cryptorchidism, sex determination and differentiation, and hermaphroditism.

The concluding portion of the volume deals with the laboratory. This part of the subject is handled briefly, in detail and yet within short compass. It includes the usual aids, endometrial biopsy and vaginal smears, sex hormone tests with description of the techniques, the hormonal findings in blood and urine, and concludes with a detailed description of the hormonal preparations available, their indication and dosage.

An authors' index is valuable in making the access to the huge bibliography easy. The illustrations, many of which are from different sources, are excellent. The entire book is satisfactory, well written and interesting. In dealing with a subject which is in such a fluid state as our present knowledge of endocrinology, it is not indicated to take exceptions to different view points which may or may not stand the test of time.

R. T. FRANK.

¹**Female Endocrinology Including Sections on the Male.** By Jacob Hoffman, A.B., M.D., Demonstrator in Gynecology, Jefferson Hospital; Formerly Research Fellow in Endocrinology and Director of the Endocrine Clinic, Gynecological Department, Jefferson Hospital, Philadelphia. Fully illustrated including some in colors. 788 pages. W. B. Saunders Company, Philadelphia. 1944.

Human Constitution in Clinical Medicine by Draper, Dupertuis and Caughey² is of interest and instructive value not only for the medical student for whom it is primarily designed, but also for every medical man, particularly for specialists who are too apt to concentrate upon one organ at the expense of the individual, not only in medicine, but also to pick the right man for the right job. To surmise what diseases an individual will be most likely to develop, constitutional factors, anthropometric measurements, photographic somatotyping, and overall correlation of features is essential. These studies deal with the essence of personal identity. The authors are well aware that some of their techniques, for instance the short cuts to the psyche, leave much to be desired, but even with these shortcomings, one should be able to predict the response of a given individual to the pressure of the whole environment, based on his personality. The foundations for this monograph were developed in the Constitutional Clinic of the Presbyterian Hospital of New York City, with aid of the Rockefeller Foundation and the Markle Foundation.

By means of methods described, one should be able to gauge the strength, the weaknesses and the qualities of a given patient, and to evaluate how much the patient himself contributes to his own disabilities. Psychiatrists have focused more upon the personal identity of the individual than any of the other disciplines in medicine. The methods for explaining the nature of Man are manifold. The response to external stimuli, be they bacterial, worry or overstrain, are different in each person. To obtain data, the authors outline the methods of history taking, with special regard to personal inheritance and personal diseases. They illustrate these methods by few but well-chosen and striking clinical examples. The same applies to every one of the methods they utilize. Among the subjects taken up are genetics as applied to clinical medicine, particularly inheritance factors and vulnerabilities. Another chapter takes up growth, development, decline and death. Under androgyny, they discuss especially nongenital attributes of sex and their variation. Anthropometry, somatypes and especially constitutional physiology are discussed.

This stimulating volume does not attempt to do more than lay the foundation for accurate observation of factors too often neglected by the clinician, and yet of utmost value in sizing up individuals, their strength and weaknesses, and how these affect the wear and tear which life entails. The book is to be highly recommended because it should stimulate further and more detailed study along these lines.

R. T. FRANK.

The second edition of Greenblatt's **Office Endocrinology**³ appears after three years. It covers a much wider field than the first edition. In fact, on looking over the index, a tremendous amount of subjects have been dealt with. It is the kind of book that contains a treatment for every ailment discussed. Apparently the most popular endocrine remedy is testosterone in one form or another. However, I am afraid a great many readers, when applying the recommended therapy, will meet with disillusion. For example, the first in the list of treatments for female sterility is, "Gentle dilatation of the cervix is frequently followed by conception. Action: a. Indirect stimulation of the ovaries. b. Promotion of cervical drainage."

R. T. FRANK.

²**Human Constitution in Clinical Medicine.** By George Draper, M.D., Associate Professor of Clinical Medicine, College of Physicians and Surgeons, Columbia University; Associate Attending Physician, Presbyterian Hospital, New York City; C. W. Dupertuis, Ph.D., Physical Anthropologist, Constitution Clinic, Presbyterian Hospital, New York City; and J. L. Caughey, Jr., M.D., Med. Sci. D., Associate in Medicine, College of Physicians and Surgeons, Columbia University. Assistant Physician, Presbyterian Hospital, New York City. 273 pages. Paul B. Hoeber, Inc., Medical Department of Harper & Brothers, New York. 1944.

³**Office Endocrinology.** By Robert B. Greenblatt, B.A., M.D., C.M., Professor of Experimental Medicine, University of Georgia School of Medicine; Director, Sex Endocrine Clinic, University Hospital, Augusta, Georgia. With a foreword by G. Lombard Kelly, M.D., Dean, University of Georgia School of Medicine. Second Edition. 243 pages. Charles C Thomas, Springfield, Illinois. 1944.

1943 Year Book of Obstetrics and Gynecology edited by Dr. Greenhill⁴ brings 565 pages of abstracts of important articles, well selected and concisely presented, in the annual literature of the two subjects. One finds here practically all of the new refinements in operations and treatments as well as the recent advances in research and clinical practice. Greenhill has devoted some fifteen pages to caudal anesthesia, and concludes with the statement that he does not believe the method will become a part of our general obstetric armamentarium. He repeats the advantages of local anesthesia for various obstetric maneuvers. There is considerable discussion of the Rh factor and the recent literature on endocrines and sulfonamides.

The book is unexcelled as a quick reference to the literature.

PHILIP F. WILLIAMS.

The report of the first **Brazilian Congress of Gynecology and Obstetrics** appears in three volumes⁵ totaling over 1,500 pages. This Congress was held at Rio de Janeiro in September of 1940, under the presidentship of Professor Arnaldo de Moraes. The Congress took up four main themes—recent advances in gynecological hormonology; the diagnosis and therapy of cervical cancer; endocrine diseases in pregnancy; and obstetrical care which includes the preconceptual, prenatal care, maternal mortality, neonatal mortality, and the social aspects and agencies.

The attendance appeared to be mainly local although some Argentine and Chilean physicians attended.

The recent advances in gynecological hormonology was introduced by a very detailed consideration of the steroid and gonadotropic hormones by Doctors Ahumada and Salaber. This likewise covered the physiology and application of these substances. The experimental and clinical aspects were treated by Salgado and Monteiro de Barros, dealing with the use of the male hormones in gynecology. A short paper by Slotta, who is now in São Paulo, dealt with the chemical aspects of the steroid.

Among the many papers on cervical carcinoma is that of Wood, Cruz and Galán. They place a great deal of value on the Schiller test and state that the earliest diagnosis of what I take to be suspected lesions, results in 100 per cent cure by mere amputation of the cervix. On the whole, they favor radiotherapy (x-ray and radium) except in radioresistant types, in which radiation is followed by radical operation.

Among endocrine diseases in pregnancy, diseases of the thyroid and parathyroid, of the adrenals, hypophysis and diabetes are taken up. In addition to the main themes, a large number of mainly casuistic reports are included. The volumes are gotten up faultlessly, are profusely illustrated, and contain the discussion. From these reports, it is evident that not only is the available material very abundant, but also that pathology, experimental investigations and therapy are on a very high level.

R. T. FRANK.

Histerosalpingografia by Buteler⁶ represents a bulky doctoral thesis. The work was done under the auspices of the University of Cordoba in Argentina. It is based on 450 cases. The monograph is illustrated profusely and adequately. The author uses iodized oil of local manufacture. He emphasizes that fluoroscopy and manometric control are essential. In special instances, pneumoperitoneum may be in-

⁴The 1943 Year Book of Obstetrics and Gynecology. Edited by J. P. Greenhill, B.S., M.D., F.A.C.S., Professor of Obstetrics and Gynecology, Loyola University Medical School, Chicago. Pages 565. The Year Book Publishers, Chicago. 1944.

⁵Anais Do Primeiro Congresso Brasileiro De Ginecologia E Obstetricia. Professor Arnaldo de Moraes, President. Vol. I, 548 pages. Vol. II, 450 pages. Vol. III, 508 pages. Jornal Do Commercio, Rodrigues & C., Rio de Janeiro. 1942.

⁶Histerosalpingografia. By Eduardo Buteler. 381 pages. Universidad Cordoba, Republica Argentina. 1943.

duced at the same time. He obtains much better pictures while the cervix is occluded. No mention of aqueous media for salpingography is made. There are many misprints of dates, as, for example, the beginning sentence in which Dartigues is supposed to have used roentgen rays in 1867.

R. T. FRANK.

The collaborators and pupils of Professor Josué A. Beruti⁷ have collected and republished all of his many contributions to the medical literature in four large volumes, totaling 2,241 pages. Acknowledgment is made to many of the pharmaceutical houses who probably have contributed. This publication commemorates the twenty-fifth anniversary of professorship at the Medical School of the University of Buenos Aires. Professor Beruti started his medical publications in the year 1902 and the collection extends to 1943 inclusive. The entire sphere of obstetrics is included, covering physiology of pregnancy, of the puerperium, pathologic deviations, operations and many subjects which embrace such diverse topics as female education, scientific propaganda and cultural diplomacy of Germany in Argentine and even funeral orations. These volumes cover the actual activities of a man of wide interests.

R. T. FRANK.

Dr. Raúl García Valenzuela has published a monograph on the **Treatment of Septic Abortions**⁸ which he utilized as the thesis for obtaining the title of clinical professor at the University of Chile. The thesis is based on 300 cases of which 52 per cent were definitely determined as of criminal origin. This covers a period of two and one-half years. There were 15 serious complications, including 3 embolic ones.

The treatment appears to consist of observation for a few days, the giving of drugs helping to contract the uterus in order to aid emptying of the cavity. Where there is persistent retention, a cautious emptying of the uterus is performed. The sulfa drugs have been used. A full discussion, particularly of the Latin American literature as well as the German sources, is given. It is noticeable that in 1,716 cases extending from 1934 to 1942, the overhead mortality has decreased from 27.9 per cent to 8.8 per cent. The monograph concludes with short case histories of 300 patients. There is nothing particularly new in the presentation.

R. T. FRANK.

The sixteenth edition of **Care and Feeding of Children** by L. Emmett Holt,⁹ appears on its fiftieth anniversary. The long continued use of this book is a memorial to its value. In these days of juvenile delinquency and wartime hysteria among adolescents, one feels that a reading, by many parents, of the chapter on "Behavior Problems," would do much toward understanding and curbing some of our present social difficulties. A chapter "How to Prevent Accidents" should be ready by all who have small children. It contains sound advice.

The present edition of this book should continue to be as popular as its predecessors.

PHILIP F. WILLIAMS.

⁷Producción Científica y Cultural de Josué A. Beruti. *Obstetricia Ginecología, Medicina Social, Cuestiones educacionales, universitarias, hospitalarias, etc. Homenaje de Sus Colaboradores y Discípulos de la Cátedra de Clínica Obstétrica y de Sus Amigos. Tomo I, 472 pages; Tomo II, 628 pages; Tomo III, 601 pages; Tomo IV, 539 pages.* Alfredo Frascoli, Buenos Aires. 1943.

⁸El Problema Terapéutico Del Aborto Séptico. By Raúl García Valenzuela, Professor de la Escuela de Obstetricia y Puericultura de la Universidad de Chile. 156 pages. Universitaria, Santiago de Chile. 1943.

⁹Care and Feeding of Children. By L. Emmett Holt, M.D. Revised and enlarged by L. Emmett Holt, Jr., M.D., Associate Professor of Pediatrics, Johns Hopkins University. Pages 314. D. Appleton-Century Company, New York and London. 1943.

Doctor Castallo and Audrey Walz have presented in **Expectantly Yours¹⁰** a pleasantly and, often, amusingly told story of maternal care.

Many obstetricians will endorse the comments on the effect of illegal abortions on mortality statistics. The "Facts of Life" are just as scientific as in any average book of the same nature but the redressing of them by the junior author makes them more easily read and understood. Little of importance has been omitted in the discussion of prenatal hygiene and labor. The comparison of various methods of analgesia should amply supply the average woman's curiosity in this matter.

The chapter entitled, "The Come Back," is excellently done, it is a good story of the puerperal state, and Doctor Castallo's wise note on birth control is well placed. For the patient who wants or needs, according to her temperament, a manual in a lighter vein with an occasional smile, and yet, with plenty of solid information, this book fills the need.

PHILIP F. WILLIAMS.

Dr. Carrington offers in **Safe Convoy¹¹** a very comprehensive textbook for the expectant mother. He has divided the material into nineteen chapters covering all phases of pregnancy, labor, puerperium and infant care. There are few questions which the pregnant woman may ask her physician that are not specifically answered in this book. Dr. Carrington states in his preface of the book that it is not intended to replace ante-partum care with the physician, but to enable the woman to understand fundamentals so that she may cooperate more intelligently with her doctor. In these busy days of obstetric practice, this book should be a boon to women unable to contact their obstetrician easily.

One likes, particularly, Dr. Carrington's discussion on analgesia and anesthesia and is in accord with his feeling that very little of these methods are necessary in the average birth. The style of presentation is delightful for Dr. Carrington illustrates almost every section with allusions to comparable situations in biblical, historical and even recent popular literature. The final chapter of the book on "Fathercraft" is an excellent inclusion. Few obstetricians ever have the chance to talk to prospective fathers. This chapter tells him what his wife's physician would like to say to him early in the pregnancy so the book may be well recommended to both father and mother of the baby to come.

PHILIP F. WILLIAMS.

The **History of Gynaecology¹²** is determined primarily by two factors, by the position of woman in society, and by the status of medicine, which itself is largely the result of the social and economic conditions of a given period and of its technology. Indeed, the more the physician knew about the anatomy, physiology and psychology of women, and about the causes and pathogenesis of disease, the more effectively he was able to help. On the other hand, it made a great difference whether woman was considered a beast of burden, the "door to hell" (*janua diaboli*), or whether she was worshipped. A history of gynecology is therefore by necessity, a combination of social and medical history.

¹⁰**Expectantly Yours.** A book for Expectant Mothers and Prospective Fathers. By Mario A. Castallo, A.B., M.D., F.A.C.S., Assistant Professor of Obstetrics, Jefferson Medical College, and Audrey Walz. Pages 110. Illustrations 14. The Macmillan Company, New York. 1943.

¹¹**Safe Convoy.** The Expectant Mother's Handbook, by William J. Carrington, A.B., M.D., F.A.C.S., Attending Gynecologist, Atlantic City Hospital. Pages 253. J. P. Lippincott Company, Philadelphia and New York. 1944.

¹²**The Genealogy of Gynaecology. History of the Development of Gynaecology Throughout the Ages, 2000 B.C.—1800 A.D., with Excerpts from the Many Authors Who Have Contributed to the Various Phases of the Subject.** By James V. Ricci, A.B., M.D., Associate Clinical Professor of Gynaecology and Obstetrics, New York Medical College; Director of Gynecology of the City Hospital, New York, etc. Chapters xxi; 578 pages. Illustrated. The Blakiston Company, Philadelphia, 1943.

The present book unfortunately does not attempt to be such a history. It follows the traditional pattern and is basically a huge and heavy compilation of undigested and frequently misunderstood data. At the beginning of every chapter the author discusses the "historical background" of the period, but his picture is always conventional and he never attempts to correlate the background with his narrative. There is no doubt that the eighteenth century was filled with diplomatic intrigues, dynastic rivalries, and interminable wars, but for an understanding of the history of gynecology, it is more important to remember the great part played by women in that century, the rise of the middle class, or the beginning of the industrial revolution which was to influence the social position of woman and her entire pathology so considerably.

The author has undoubtedly devoted much time and labor to the preparation of his book. His bibliographies look very impressive, but unfortunately he worked a great deal from secondary sources and used good and bad books, modern scholarly studies and outdated uncritical monographs, without any discrimination. Hence, when he happens to follow a good source his statements are correct, but when the source is bad, he does not hesitate to tell the most fantastic stories. Thus he still believes that the early temples of Æsculapius were medical schools and mentions Epidaurus, Cos and Cnidus in one breath (p. 47). Being unaware of the archeological literature on Cos, he still thinks that there was a temple of Æsculapius on that island at the time of Hippocrates (p. 52), while the excavations of Herzog have demonstrated unmistakably that the cult of Æsculapius was not introduced before the middle of the fourth century B.C., that is, after Hippocrates' death, and that the temple was built in the beginning of the third century.

Speaking of Salerno, the author states that the Salernitan masters of the twelfth century "did not take kindly to Arabic influences" (p. 244). The contrary is true. He mentions among others Nicolaus Praepositus, but if he had known a study of Wickersheimer published in 1911, he would have found that Nicolaus Prepositi was a sixteenth century French physician;* and if he had known a book that I wrote over twenty years ago,† he would have seen that the Salernitan Antidotarium Nicolai is conspicuous for its Arabic influence. It would be easy to point out dozens of similar mistakes due to mere ignorance of the basic literature.

Wrong dates are always disturbing, but particularly so when a date marks a turning point. The illustration of the female genitalia from Johannes de Ketham (p. 287) is not from the edition of 1491, and this is precisely why it is significant. The edition of 1491 had a totally different, purely diagrammatic, traditional illustration, while only two years later, the publisher felt that he could no longer present the public with such mediaeval pictures and had a new, realistic one drawn by a Renaissance artist, the picture that is found in the various editions from 1493 on.

One cannot help feeling that the author has not read all the sources he quotes. When he gives the title of a book in Greek characters, every accent is wrong (p. 205); when he quotes Latin texts and omits the verbs or other crucial words, so that the sentence does not make sense (pp. 251, 289); when he refers to Pseudo-Apuleius as Apuleius Barbatus, the bearded Apuleius, instead of Apuleius Barbarus, as he was sometimes wrongly called (p. 168), it certainly sounds strange.

It is highly regrettable that the author did not consult the best history of ancient gynecology that has ever been written, that of Paul Diepgen, a book that was published in 1937, and that can be found in every large medical library.‡ Diepgen

*Ernest Wickersheimer, Nicolaus Prepositi, ein französischer Arzt ums Jahr 1500. *Archiv für Geschichte der Medizin*, 1911, Vol. V, pp. 302 ff.—*Bulletin de la Société Française d'Histoire de la Médecine*, 1911, Vol. X, pp. 388-397.

†*Studien und Texte zur frühmittelalterlichen Rezeptliteratur*. Leipzig, Johann Ambrosius Barth, 1923 [Studien zur Geschichte der Medizin herausgegeben von der Fuschmann-Stiftung an der Universität Leipzig, Heft 18].

‡Die Frauenheilkunde der alten Welt. In: *Handbuch der Gynäkologie*, herausgegeben von W. Stoeckel, 12. Band, 1. Teil, München, 1937, Verlag von J. F. Bergmann, 348 pp.

has practiced gynecology for many years, and is one of the most distinguished and most competent medical historians of our time; professor of the history of medicine and director of the Berlin Institute since 1930. His book is the result of thirty years of historical research, is based entirely on original sources and fully documented. If our author had taken the trouble to compare his findings with those of Diepgen and had looked up the sources quoted by Diepgen, he would have been spared an endless number of mistakes.

Another shortcoming that must be mentioned and for which the publisher is as much to blame as the author, is the fact that the book has literally hundreds of typographic errors. French words possess accents; this may be unpleasant, but the accents cannot be disregarded. German words are inflected and wrong endings may change the meaning of a sentence. The book looks as if it had been printed without any proofreading from an uncorrected manuscript.

It is very discouraging to see such books published at a time when great efforts are made to raise the standard of medical historiography, and when institutions are available where a student can seek expert help and advice. An amateur can make valuable contributions to the history of medicine, provided he is aware of his limitations and selects a subject that he is equipped to handle. A history of gynecology that covers 3,800 years of human civilization is the most ambitious task that a historian can set for himself. It requires not only gynecologic knowledge, but a complete mastery of the methods of historical research, and the writer of such a book must be equally at home in the fields of anthropology, Oriental philology, classics, mediaeval, Renaissance and modern studies.

It will take years of effort to eradicate the mistakes that this book is perpetuating.

HENRY E. SIGERIST.

Miscellaneous

Psychosomatic Medicine,¹³ written by an internist trained in psychological medicine, and a psychiatrist with wide experience in the field of general medicine, deals with the clinical application of psychopathology to general medical problems.

After a short but inclusive chapter devoted to personality development and psychopathology, the authors consider in systematic fashion the psychosomatic aspects of the disorders and diseases of the various bodily organs and systems. The glands of internal secretion and their relation to personality disturbances; the sexual function and its relation to general medicine; such common problems as headache, constipation and sleeplessness are dealt with from the standpoint of their emotional implications.

Perhaps the most valuable section of the book is that portion which deals with treatment. Here methods of eliciting a psychosomatic history, the presentation of the explanation of psychosomatic illness to the patient and the general principles of psychotherapy are discussed. A useful chapter discusses such common "normal" problems in psychotherapy as the feeding problems of infancy and childhood, sexuality of childhood, problems of adolescence, marital maladjustments and divorce, the psychology of pregnancy and parturition and the psychosomatic problems of aging. All of this material will be of interest to the obstetrician and gynecologist.

The last World War gave great impetus to the development of modern psychiatry. The publication of this timely book suggests that the present World War will provide the basis for a more final integration of psychiatry into general medicine, in other words, what is here spoken of as psychosomatic medicine.

PHILIP F. WILLIAMS.

¹³**Psychosomatic Medicine.** The Clinical Application of Psychopathology to General Medical Problems. By Edward Weiss, M.D., Professor of Clinical Medicine, Temple University Medical School, Philadelphia, and O. Spurgeon English, M.D., Professor of Psychiatry, Temple University Medical School, Philadelphia. Pages 659. W. B. Saunders Company, Philadelphia and London. 1943.

This comprehensive text, 766 pages, **The Hospital in Modern Society** by Bachmeyer and Hartman¹⁴ is a collection of material from the literature for those interested in hospital administration. These articles have been carefully selected and adopted. Unfortunate delay in publication has prevented the inclusion of articles subsequent to 1940, although bibliographies for most chapters have been brought up to July, 1943.

The book is divided into five parts, taking up the origins and use of hospitals; organization and management of hospitals; the medical and nursing staffs as well as the special intramural services, financial, maintenance, administration, and public health aspects; and, finally, the relationship of hospital to community and public health. The various chapters in this part of the book are composed of adaptations of discussions of specific hospital problems as they have appeared in the literature and each section answers the question that may be brought up by the various personnel staffs of the institution.

The chapter on obstetric services contains articles by Dr. Bingham, Miss Konrad and Dr. Cornell. Although these articles are dated several years previously, they are just as effective today as when they were written. Other chapters of interest to medical services, at least, should be those regarding the operating room, x-ray, laboratory and other sections of the hospital with which the physician comes into daily contact.

The chapter on legal aspects should be read by all medical staff members. Not the least interesting parts of the book are the discussion of group hospital and health insurance, and the chapter on public health. It is to be regretted that these sections are not up to date, in view of the developments in these fields in the last few years. One regrets particularly, the section by Dr. Thomas Parran entitled, "Next Objectives," could not have been rewritten in recent months.

The volume is really a most important book for all hospital libraries, and for those both lay and professional, who wish to comprehend the underlying problems of hospital administration and management.

PHILIP F. WILLIAMS.

Standard Nursing Procedures of the Department of Hospitals, City of New York,¹⁵ was prepared by a Committee of Nurses advised by numerous physicians. It may be considered a reference book, which should be of use to all who are instrumental in teaching nursing, as well to administrators of hospital nursing. A very interesting history of the development of the department of hospitals in New York City begins the volume. The first almshouse in New Amsterdam was opened in 1653. The first private hospital may be said to date from 1660 when the Dutch West India Company built it for its slaves, seamen and soldiers. In 1784, the close of the Revolution, the New York hospital system for the poor may be said to have originated.

A detailed guide for basic nursing care covers more than 300 pages. Special nursing procedures include obstetric nursing, nursing of infants and children, and the basic procedures in neurological nursing. This detailed guide concludes with a short chapter on the hospital in the community, written by Bernecker, the present Commissioner of the Department of Hospitals.

The text is arranged for rapid orientation and for obtaining detailed information readily. While the average nurse will find the contents too voluminous, it will prove of great assistance to supervisors and teachers.

R. T. FRANK.

¹⁴**The Hospital in Modern Society.** Edited by Arthur C. Bachmeyer, M.D., Director, University of Chicago Clinics, Director, Hospital Administration Course, University of Chicago, and Gerhard Hartman, Ph.D., Director, Newton Hospital, Newton Lower Falls, Mass. Pages 766. The Commonwealth Fund, New York. 1943.

¹⁵**Standard Nursing Procedures of the Department of Hospitals, City of New York.** Prepared by the Committee of Nursing Standards, Division of Nursing, Department of Hospitals, Mary Ellen Manley, R.N., M.A., Director. 436 pages. The Macmillan Company, New York. 1943.

The aim of this book, *Applied Dietetics* by Frances Stern,¹⁶ is to present a procedure for planning and teaching normal and therapeutic diets. The book is divided into four parts which take up the construction of such diets, tables for computing diets, a series of dietary outlines for the treatment of various diseases, and an illustration of how food prescriptions may be filled.

There are two very important chapters in Part I—the education of the patient on a normal diet, which should give physicians and others concerned many ideas on lay education in nutrition. The following chapter continues the same ideas as applied to therapeutic diets. Such advice as given here should be very helpful.

There have been many advances in nutrition since the first edition in 1936, and one will note here most recent findings concerning the vitamins, mineral values of foods and vitamin deficiencies. It is stated that the section on diabetes has been completely revised.

As far as the obstetrician is concerned with nutrition, he will find here excellent material on the nutritional needs of pregnant women both in the normal state and where complications are present. There are sample diets for pregnant patients with chronic nephritis, pernicious vomiting, and for eleven other abnormal conditions which are frequently found associated with pregnancy. Since the majority of pregnant women are either overweight or underweight, the obstetrician may find some excellent material on the chapters on obesity and underweight. All these sample diets for pregnancy or complicating diseases are worked out in terms of menus as well as nutritional factors.

The book should be of interest and value to many groups of professional people who are interested not only in normal nutrition and in prescribing dietary therapy for various diseases and conditions.

PHILIP F. WILLIAMS.

The second edition of *Pioneers of Pediatrics* by Dr. Levinson,¹⁷ within seven years, shows that this book actually has met a demand. The subject matter covers children's disease and children's care from the earliest time, beginning with Hippocrates, who described mumps, and covering the Islamic, the fifteenth to eighteenth centuries, then proceeding up to the present time. Some of the high marks are Jenner's introduction to vaccination; Heine, who in the nineteenth century described poliomyelitis; the work of Holmes, Semmelweis, Credé, Hutchinson, Barton, von Behring, Still, von Pirquet and Schick. The pioneers of infant feeding, those who investigated alimentary disturbances are mentioned, and finally the American pioneers of pediatrics. Only very few living physicians are included. There are numerous full-page portraits which add to the value of this brief abstract of history.

R. T. FRANK.

¹⁶*Applied Dietetics.* The Planning and Teaching of Normal and Therapeutic Diets. By Frances Stern, Chief of Frances Stern Food Clinic, The Boston Dispensary, Assistant in Medicine, Tufts College Medical School. Second Edition. Pages 225. Tables 57. The Williams & Wilkins Company, Baltimore. 1943.

¹⁷*Pioneers of Pediatrics.* By Abraham Levinson, B.S., M.D., Assistant Professor Pediatrics, Northwestern University Medical School; Professor of Pediatrics, Cook County Graduate School of Medicine; Attending Pediatrician, Children's Division of the Cook County Hospital; Senior Attending Pediatrician, Sarah Morris Hospital for Children of the Michael Reese Hospital; Senior Attending Pediatrician, Mount Sinai Hospital, Chicago. Second Edition; Foreword by I. A. Abt. 119 pages. Froben Press, New York. 1943.

Correspondence

The Role of the Physician in Child Adoption

To the Editor:

Although proper procedures for child adoption are available, they differ unfortunately in various states. Moreover, such information is scattered either throughout numerous periodicals, or else is contained in special books with limited distribution and publicity. A sad incident in this connection, which undoubtedly occurs more frequently than is usually recognized, took place recently with which I, as the obstetrician handling the case, was personally involved. My experience in this instance is worthy of dissemination to others who may be confronted some day with a similar problem.

An unmarried, pregnant primipara was referred to me for obstetrical care. Owing to religious tenets, she was accordingly desirous of giving birth to the baby, but subsequently planned to place the child in the hands of adoptive parents. During the entire ante-partum period, through the power of suggestion, I tried to stimulate her to keep the child herself when it arrived so that it might receive the love and affection of its own mother. She remained determined in her wish "to give the child away" soon after its birth, even to the point of refusing to see the child when it would be born.

In due time, a normal male child was uneventfully delivered. While the patient was in the hospital following delivery, I again tried to impress upon her the advisability of bringing up the child herself but to no avail. She stubbornly refused even to see the child and insisted that it be given for adoption.

The problem of a suitable disposition of the child then arose. The expressed desire of the patient was that it be placed directly in the home of adoptive parents without the intervention of any religious, social or welfare agency. Although the advantages of adoption committees were explained to the mother, for some reason or other she did not entertain the idea for even a moment. She seemed to be of the belief that the particular social or religious agency in this State (New York), to which the child would be forwarded, might send her baby to a "home" or an orphanage. I could not change her mind and unfortunately allowed myself to consent to her wishes for "private adoption." One of my medical colleagues contacted me about obtaining this child for a member of his family whose marital life was barren and although I was reluctant to be a party to a private adoption, he could see no ill effects from it. Despite my warning that in this State the mother could always claim the child at any time prior to granting of the final and legal adoption papers by the Surrogate's Court (a six-month period of time must elapse during which investigations are made of the conditions in the home of the adopting parents before obtaining permanent and legal parenthood of an adopted child), the physician for the adoptive parents minimized such an occurrence. He explained that he had fully acquainted the prospective parents with the possibility of the mother changing her mind but that they were willing to chance the risk.

Accordingly, the mother willingly gave temporary custody of the child to the new parents through the necessary papers arranged by their attorney and the child was taken from the hospital and delivered to its newly-acquired parents. The ten-day-old infant was immediately accepted gratefully as a member of the household.

A trained baby nurse was placed in complete charge of the baby and the child prospered. The love and affection of the adoptive parents for the child steadily grew. Not only the "parents" but even the "grandparents" of the baby were completely enthralled by the baby, so much so that the manner of its accession had been quite forgotten.

All seemed well, but like the calm before the storm all was not well. At about this time, my patient appeared at the office (three months post partum) and with determined resolution stated that she wanted the child returned to her. She informed me that she was well within her legal rights and that during the past three months she had sufficient time for reflection. Her decision to claim the child was definite and any attempt of mine to now interfere was futile (since I had constantly urged this very thing during the months prior to confinement). I made her wishes known to the other physician. The adoptive parents contested the action in court but in the end, the child was returned to its true mother. It is needless to describe the extreme hurt which the adopting mother and father experienced.

It is not within the province of this correspondence to take issue with the decision of the court since the law of the state is clear and the verdict was technically justified. The real reason for telling of this experience is to acquaint the profession with the proper method of child adoption. If there exists in the respective state in which the physician resides an agency or adoption committee especially devised for this purpose, the doctor *should insist* upon such an agency handling the adoption of a baby. Such stories as I have related are not uncommon, they are far too frequent as close scrutiny of court records will disclose. Social agencies and specialized adoption committees that have studied the problem certainly are far better equipped to make decisions in this matter than physicians, who are ignorant of the possible consequences. In the final analysis, the physician is a highly trained technician whose education in welfare work has been neglected, while welfare agencies have improved to such an extent that the states of our Union have seen fit to grant them special privileges in the handling of children for adoption which obviates such cruel episodes as suffered by all involved in the case described above.

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Society Transactions

NEW YORK OBSTETRICAL SOCIETY

MEETING OF NOVEMBER 9, 1943

The following paper was presented:

Some Observations on the Use of Caudal Analgesia in Obstetrics. Clifford B. Lull, M.D. (by invitation). (For original article, see page 312, March, 1944, issue.)

MEETING OF DECEMBER 14, 1943

The following papers were presented:

Transplantation of Abdominal Fascia for the Relief of Urinary Stress Incontinence. William E. Studdiford, M.D. (For original article, see page 764.)
Endometriosis Interstitiale With a Report of Three Cases. James R. Miller, M.D., and Robert Tennant, M.D. (For original article, see page 784.)

MEETING OF JANUARY 11, 1944

The following papers were presented:

A Previllous Human Ovum Accidentally Recovered in a Curettage Specimen. Andrew A. Marchetti, M.D.
The Elderly Primipara. Katherine Kuder, M.D. (by invitation), and Donald G. Johnson, M.D. (by invitation). (For original article, see page 794.)

MEETING OF FEBRUARY 8, 1944

The following papers were presented:

Congenital Vaginal Occlusion of the Cervix: Report of 2 Cases. Walter T. Dannreuther, M.D. (For original article, see page 826.)
Carcinoma Subsequent to Radiotherapy for Benign Uterine Conditions. James A. Corscaden, M.D., John W. Fertig, M.D. (by invitation), and S. B. Gusberg, M.D. (by invitation).

THE OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF FEBRUARY 3, 1944

The following paper was presented:

Supravesical Extraperitoneal Cesarean Section: A Review of the Anatomy and Technique, and Results in 250 Cases. Edward G. Waters, M.D.

PITTSBURGH OBSTETRICAL AND GYNECOLOGICAL SOCIETY*MEETING OF FEBRUARY 7, 1944*

The following papers were presented:

Classification of Toxemia of Pregnancy. Paul Titus, M.D. (For original article, see page 817.)

Carcinoma of the Ovary. Samuel Goldstein, M.D. (To be published.)

BROOKLYN GYNECOLOGICAL SOCIETY*MEETING OF FEBRUARY 4, 1944*

The following paper was presented:

"John Osborn Polak, M.D." A Memorial Address. Alfred C. Beck, M.D.

Erratum

In the article entitled "Caudal Analgesia: An Experimental and Anatomical Study," by Virginia Singleton Lanier, M.D., Howard E. McKnight, M.D., and Mildred Trotter, Ph.D., St. Louis, Mo., which appeared in the May issue, page 635, the positions of the outlines of the vertebral columns depicted in Fig. 1 should have read:

"The letters A and B should have been interchanged."

Necrology

WILLIAM SIDNEY SMITH, M.D., F.A.C.S., Diplomate of the American Board of Obstetrics and Gynecology, Graduate of the College of Physicians and Surgeons, New York, 1905, Chief Attending Gynecologist and Obstetrician of the Brooklyn Hospital, died suddenly on April 17, 1944, at the age of 61.

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